VOLUME 80 * DECEMBER 1958 * NUMBER 6

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INDEX NUMBER

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REGULAR DEPARTMENTS

A. M. A.
Archives of Neurology and Psychiatry

VOLUME 80 DECEMBER 1958 NUMBER 6

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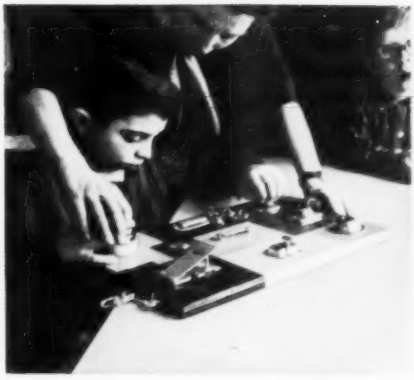

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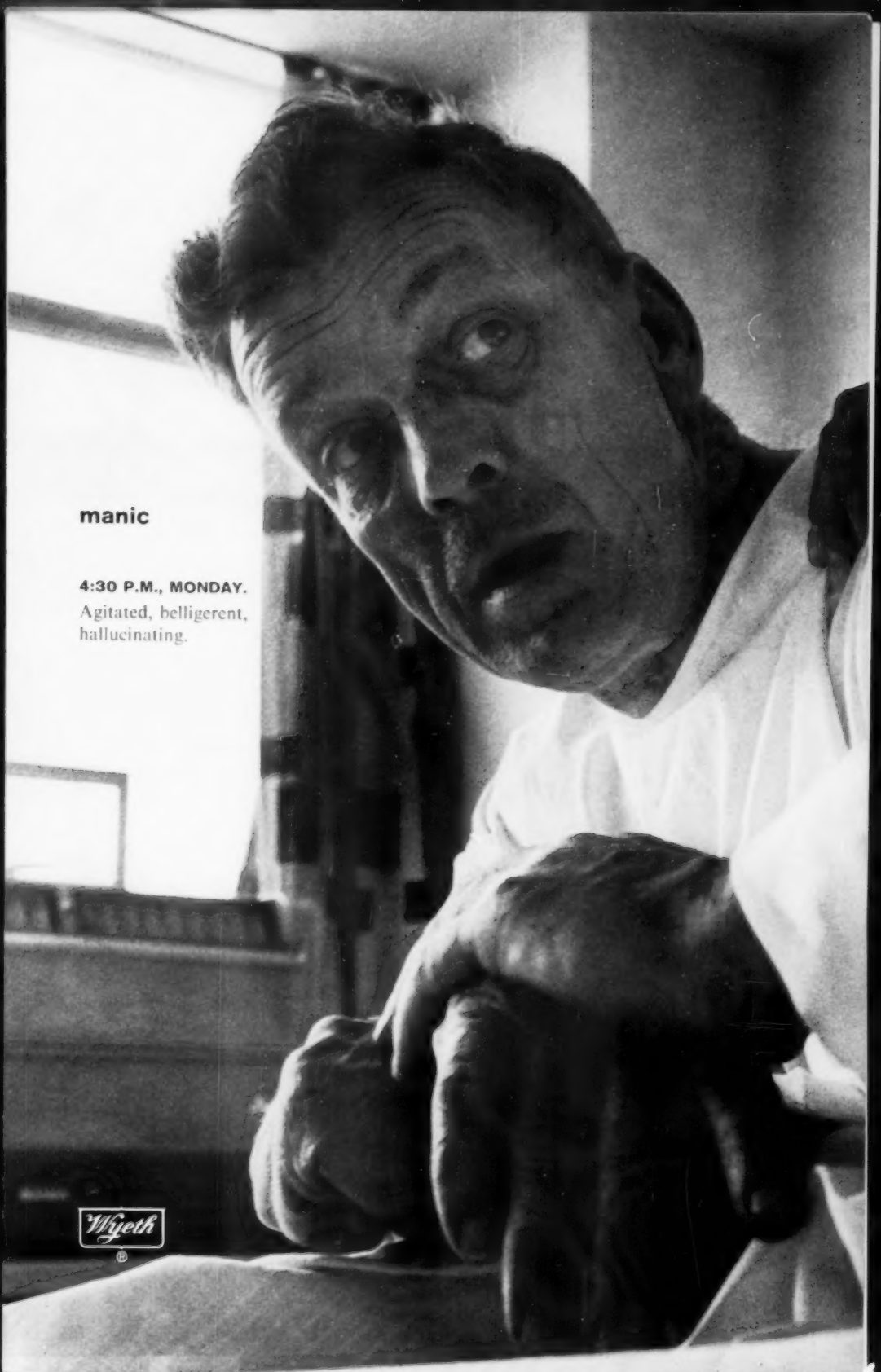
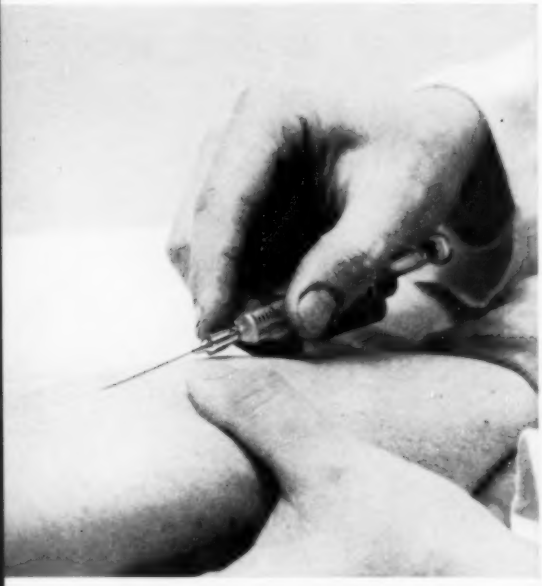
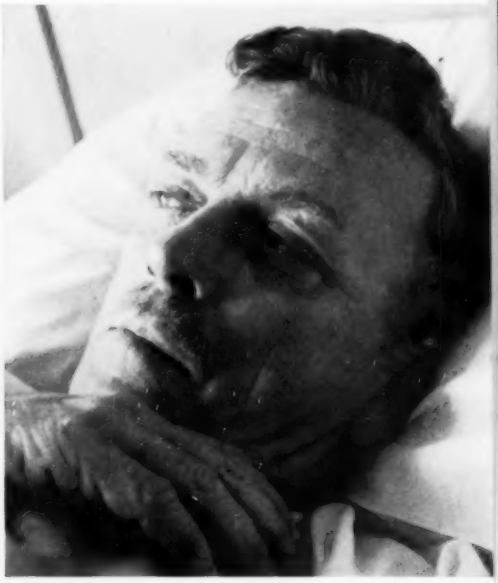

manic
4:30 P.M., MONDAY.
Agitated, belligerent, hallucinating.
Wyeth

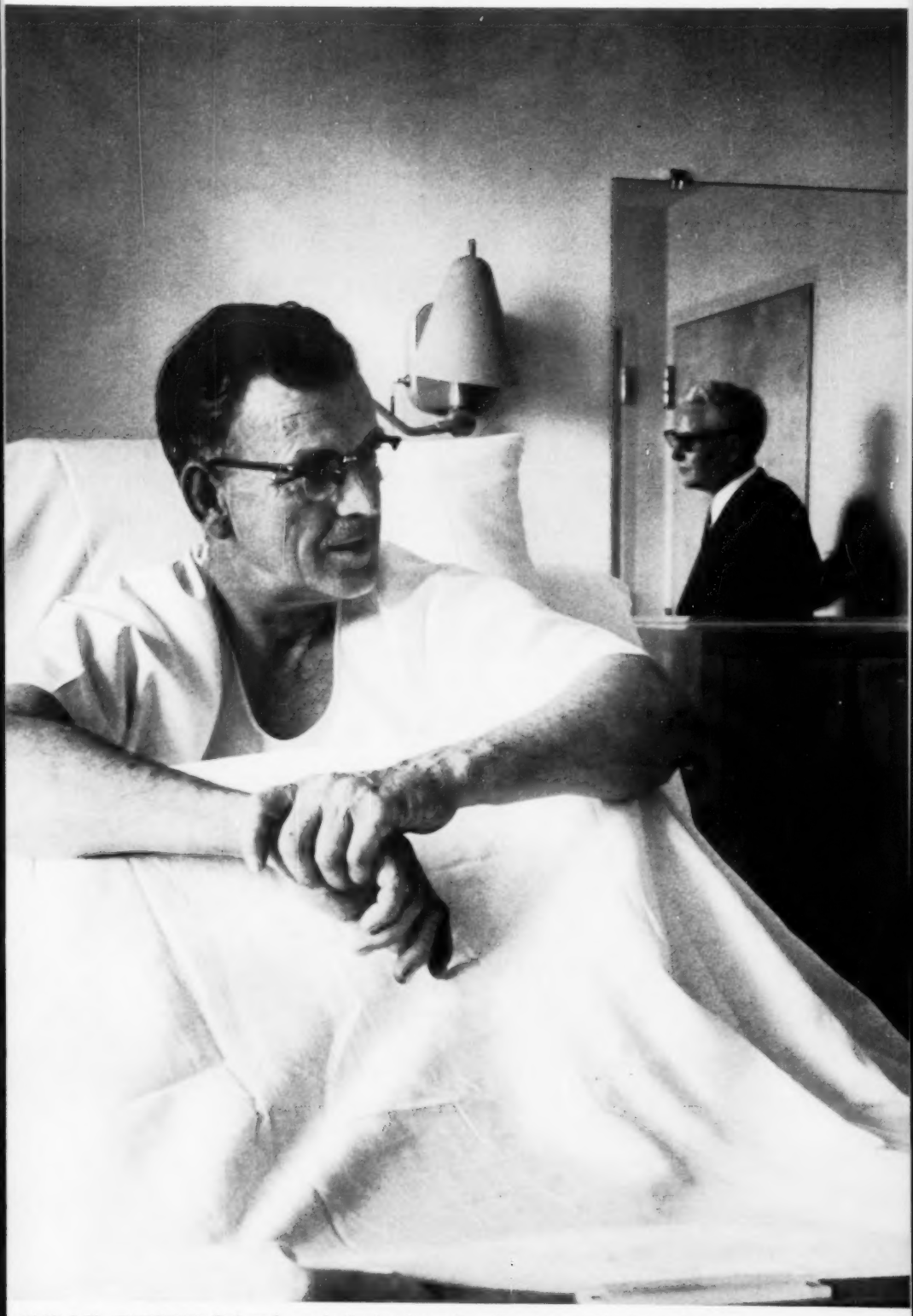
4:40 P.M., MONDAY. SPARINE I.V.



5:00 P.M., MONDAY. Calmer, less hostile. cooperatively to questions.



7:30 A.M., TUESDAY. Refreshed but some agitation remains. SPARINE I.V.



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1. Alexander, L.: Chemotherapy of depression—Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. 2. Current personal communications; in the files of Wallace Laboratories.

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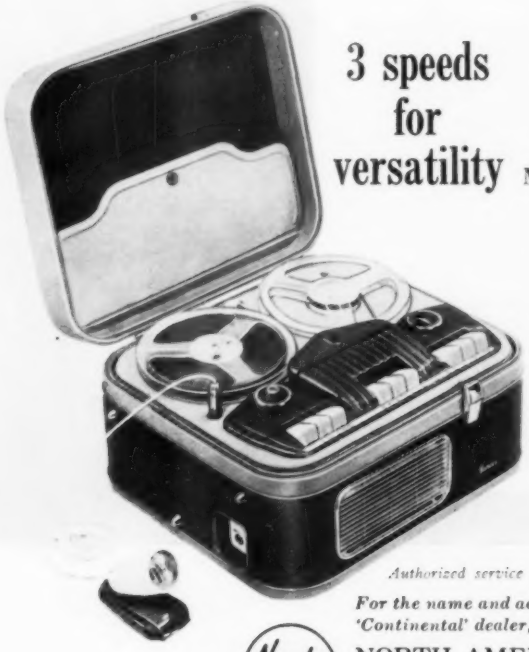

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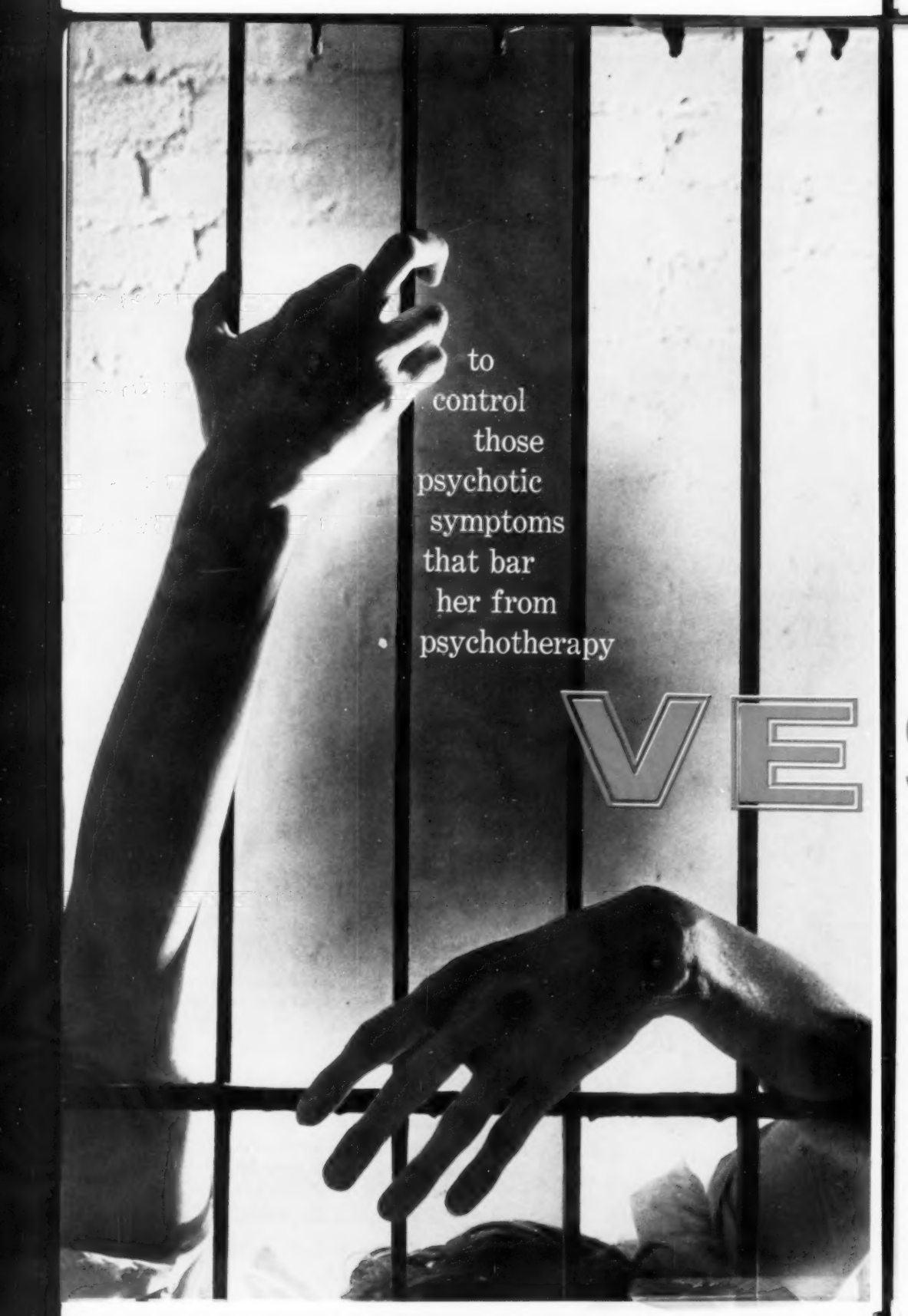
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1. Graffagnino, P. N., Friel, P. B. and Zeller, W. W.: Emotional disorders treated with meprobamate and promazine. Connecticut M. J. 21:1047, Dec. 1957.

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(hospitalized patients—all types)

by disease

DIAGNOSIS	NO. OF PATIENTS	NO. IMPROVED
SCHIZOPHRENIA		
PARANOID	7	2
NON-PARANOID	45	34
DEPRESSION		
PSYCHOTIC†	37	25
NEUROTIC	16	10
ANXIETY STATE	9	8
CHARACTER DISORDERS	15	13
OTHERS	16	13
TOTALS	145	105

by symptom

SYMPTOM	NO. IMPROVED
SLEEP DISTURBANCES	36
ANXIETY	30
TENSION	31
AGITATION	8
OTHERS	11
TOTAL	116

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Multiple Sclerosis in Twins and Their Relatives

Preliminary Report on a Genetic and Clinical Study

ROLAND P. MACKAY, M.D., and NTINOS C. MYRIANTHOPOULOS, Ph.D., Chicago

The increasing search for the causes of multiple sclerosis has led in the past two decades to a close reexamination of the old idea that constitutional or genetic factors may play some role in the etiology of this disease. The evidence currently presented for or against a hereditary background for multiple sclerosis comes chiefly from three sources: (*a*) reports in the literature of more than one case in a family; (*b*) genetic studies involving the relatives of patients with the disease, and (*c*) observations of twin cases.

During the past 60 years instances of more than one case in a family have been reported with increasing frequency.[1] The genetic studies were initiated, so to speak, by the pioneering work of Curtius[2] and Curtius and Speer.[3] Three or four other genetic studies followed. Findings in these studies do not differ greatly from one another and are summarized in a table later. A few cases of multiple sclerosis in identical and fraternal twins have been reported in the literature, but only one systematic study was done, that of Thums,[4] in Germany. Unfortunately, Thums presented no evidence whatsoever concerning the zygosity of his twins.

Accepted for publication Jan. 10, 1958.

This investigation was supported wholly by Grant No. 87 from the National Multiple Sclerosis Society.

Professor of Neurology, Department of Neurology and Neurological Surgery, University of Illinois College of Medicine, and St. Luke's Hospital (Dr. Mackay). Research Associate, Department of Neurology and Neurological Surgery, University of Illinois College of Medicine, and Dight Institute for Human Genetics, University of Minnesota (Dr. Myrianthopoulos).

Epidemiologic Characteristics of Multiple Sclerosis

The peculiar epidemiologic characteristics of multiple sclerosis will be described briefly, since a comparison with the findings from our sample will be called for later.

The prevalence and incidence of the disease cannot be adequately discussed without reference to its well-known increased distribution in the higher latitudes of the temperate zones. It seems advisable that the figure of 1 in 2000 be chosen as the most representative general prevalence of the disease in the United States and Canada.[5] Earlier investigators were of the opinion that multiple sclerosis had no predilection for either sex, but Kurland and Westlund,[6] in their careful and fairly complete epidemiologic surveys, reported a consistent excess of affected females over males with respect to prevalence, incidence, and mortality rates, by a ratio ranging from 1.2:1 to 2.4:1.

The present report is a preliminary account of the detailed study of 54 pairs of twins, who volunteered in response to our request that at least one of them must have multiple sclerosis, and of their relatives.

Our purpose was primarily to compare the rate of concordance among monozygotic with that among dizygotic twins and to compare the prevalence of the disease among the close relatives with that in the general population. At present the investigation, although not quite complete, is sufficiently advanced to permit a report of our findings. Unfortunately, case descriptions must be omitted from this preliminary report. They will be included in full in the final report.

Methods

To secure the twins for this study, the National Multiple Sclerosis Society advertised in 1954 and 1955 in newspapers, magazines, and by radio for twin pairs with multiple sclerosis in one or both members of the twinship. Unfortunately, through an error, requests at first were for identical twins, but later for any twins. As a result, a gradually increasing number of twin-pairs were secured, now totaling 76, scattered over the United States and Canada. Every twin was required to complete a questionnaire concerning his personal and medical history, place of birth, successive residences, dietary habits, and occupations, as well as a list of his relatives, indicating any with neurologic abnormalities. The relatives were then approached directly and asked to complete a questionnaire on their families and medical history.

Exhaustive efforts were then made to study every twin both genetically and neurologically. Genetic studies were directed toward establishing the type of zygosity in each twinship by comparing the two members with respect to (1) physical characteristics, (2) fingerprints, and (3) major and minor blood groups, including ABO, MN, CDE ce, Kell, Duffy, and Lewis. None of these diagnostic aids, except the blood groups, is an accurate diagnostic index for zygosity because a large amount of subjective judgment enters into their interpretation. Recently Smith and Penrose [7] devised an excellent method for objective evaluation of the probability of zygosity, based on empirical figures of the frequency of these various characters in the population. This method, which is too complex to present here, was employed for the determination of zygosity in all twin pairs except three, in which the affected twin was dead. Since blood groups and fingerprints could not be obtained for both twins in these cases, we were obliged to rely on the subjective evaluation of physical characteristics, supported by the performance of the twins in grade and high school. We thus determined that one pair of these twins is monozygotic and the other two dizygotic.

Concurrently with the genetic studies, neurologic appraisal was carried out on every twin by securing reports on any previous medical, neurologic, or cerebrospinal fluid examination, and then through reexamination of every such person, either by one of us (R. P. M.) or by a carefully selected and thoroughly competent neurologist, the examination including again, wherever possible, study of the cerebrospinal fluid for content of γ-globulin, as well as by routine methods. The estimations of γ-globulin were all done by Dr. Elvin A. Kabat, of Columbia University, in order to assure uniformity of procedure. Finally, all relatives with neurologic abnormalities were subjected to the same procedure of neurologic examination.

Not all of the 76 pairs of twins could be used for the purposes of this study, because some of them proved not to have multiple sclerosis and some withdrew their initial cooperation. Clinical and genetic work is still going on in some cases. A classification of the sample as of this date is given in Table 1.

The sample, therefore, consists of 63 pairs of twins, 9 of which are still being studied. The description of the characteristics of the twins and the genetic analysis will be confined to the completed 54 pairs, although the addition later of 9 pairs may alter the picture somewhat.

Of the 54 pairs, 29 proved to be monozygotic and 25 dizygotic. Of the 25 dizygotic

TABLE 1.—*Classification of Seventy-Six Pairs of Twins as of Date of Study*

	No. of Pairs
Studies complete	54
Studies incomplete	9
Excluded	
Not multiple sclerosis	5
Nonaffected twin dead	3
Cooperation withdrawn	5
Total	76

pairs, 21 were like-sexed and 4 unlike-sexed. Of the 50 over-all like-sexed pairs, 40 were female and 10 male pairs. In terms of affected index cases, there were 43 affected females and 11 affected males, or a ratio of almost 4:1.

Perhaps there has never been such a thing as a perfect sample in human genetics, nor is there likely to be one until our methods become more refined. An ideal sample of twins should satisfy the following two criteria: (1) It should be an unbiased selection of twins from an unselected series of affected persons in a population, and (2) it should be a miniature twin population, with the various types of twins proportionately represented as in the parent population, assuming, of course, that the trait under study is randomly distributed to an equal degree among twins and nontwins.

It becomes at once evident that the first criterion has not been fulfilled because of the mode of selection. With respect to the second criterion, it is well known from many investigations that about one-third of all twins born in the United States and Canada are monozygotic and that the proportion of like-sexed to unlike-sexed dizygotic twins is 1:1. Our sample is not in good agreement with this distribution of twins in the population. The observed proportion of monozygotic to dizygotic twin pairs is 29:25, or a ratio of 1.15:1, as against a ratio of 2:1 in favor of dizygotic pairs in the population. The observed proportion of like-sexed to unlike-sexed among the dizygotic pairs is 21:4, or a ratio of 5:1, as against a ratio of 1:1 in the population. Clearly, the sample is weighted in the direction of monozygotic twin pairs, and of like-sexed pairs among the dizygotic. It will be recalled that the ratio of female to male index cases was 4:1. This ratio, although depicting an excess of females over males larger than any heretofore reported, shows this excess to be in the same direction as that found by Kurland and Westlund[6] and Stover.[8] We suspect that our request for volunteers reached and appealed to more women than men. Finally, an inspection of the geographic location of index cases shows good agreement with the peculiar geographic distribution of the disease, and it further reflects rather well the over-all distribution of the population in the United States and Canada.

It is evident, then, that while the sample is a poor representative of the twin population, it agrees fairly well with some important epidemiologic features of multiple sclerosis, such as predilection of one sex over another and geographic distribution.

The nonrepresentativeness of the sample can readily be attributed to the original request for "identical" twins and to unavoidable difficulties in sampling technique. The assumption made with respect to the second criterion, that, in the general population, the disease is randomly distributed to an equal degree among twins and nontwins, is a heavy one, and, in view of the complex biology of twinning, probably difficult to defend.

The ideal standards for the neurologic diagnosis of multiple sclerosis in this investigation were those suggested by one of us (R. P. M.)[1] in a previous study. It was thoroughly recognized that the diagnosis of multiple sclerosis is often exceedingly difficult, and that adherence to a rigid formula would exclude many genuine cases. Therefore flexibility of criteria must be utilized to match the pleomorphic clinical and laboratory manifestations of the disease. As we shall see, this diagnostic difficulty introduces a major problem in such a study as ours, and necessitates a classification of cases into at least three categories: definite

multiple sclerosis, possible multiple sclerosis, and normal. In the final communication detailed case reports will be presented in all crucial instances so that the reliability of our diagnosis can be appraised. Only by such a procedure can our work be shielded from the criticism of the subjective bias of "diagnosis by intuition." By the same token, it is evident that any errors we have made in the diagnosis of multiple sclerosis are on the side of conservatism, and that the occurrence of concordance among the twins and the existence of multiple sclerosis among the relatives have been underestimated, rather than overestimated, in our figures.

Results

(A). Results from the Twin Sample.—Our results can be analyzed most conveniently by considering separately the study of the twins and that of their relatives. The findings in the twin study are summarized in Table 2.

TABLE 2.—*Multiple Sclerosis in Twins*

Twin-Study Results	Monozygotic	Dizygotic
Definite M. S., fully concordant	2	1
Possible M. S., fully concordant	2	0
Definite M. S., possibly concordant	3	3
Definite M. S., discordant	22	21
Totals	29	25

It will be noted that among 29 monozygotic pairs we have discovered only 2 fully concordant pairs with unquestionable multiple sclerosis, whereas of 25 pairs of dizygotic twins 1 fully concordant pair was found. Two additional pairs of monozygotic twins were fully concordant, but for a disease which, on neurologic grounds, is only doubtfully multiple sclerosis, though well advanced. In both these instances the disease was manifested by pyramidal-tract lesions, doubtful cerebellar involvement, and no sensory disturbances after many years—abnormalities which might be due to multiple sclerosis, but, on the other hand, might not. In three other pairs of monozygotic twins and in three pairs of dizygotic twins multiple sclerosis was unquestionable in one member of each twinship, while neurologic abnormalities consistent with, but inadequate for, the diagnosis of multiple sclerosis were discovered in the other member. These twinships may thus be considered questionably concordant for multiple sclerosis. The remainder, 22 monozygotic and 21 dizygotic pairs, all exhibited clear-cut multiple sclerosis in one member of the twinship and essential normality in the other. Our results may therefore be expressed as (1) conservatively considered or (2) liberally considered. If one prefers the conservative standard of judgment, only 2 out of 29 pairs of monozygotic twins, and 1 out of 25 dizygotic pairs, were concordant. However, if a liberal attitude be adopted, one may say that concordance was found in 7 out of 29 pairs of monozygotic twins and in 4 out of 25 pairs of dizygotic twins. From a preliminary inspection of the other various characteristics of the twins, it appears that there is no association between the occurrence of multiple sclerosis and birth order within a twinship, birth order within a sibship, occupation, socioeconomic status, nationality background, religious affiliation, general activities, or dietary habits.

(B). Results from the Study of Relatives.—The selection bias involved in obtaining the twin sample has been elucidated above. This bias disappears with the study of the relatives of the twins, for they represent an unselected series of persons who came into the study because they had some specified relationship with the propositus. The bias, therefore, resulting from whatever reasons brought the propositus into the study, does not apply to them.

In order to study the relatives, we must define the propositi. In the case of monozygotic twins, both twins in the twinship are considered as *one* propositus, since they are genetically alike. In the case of dizygotic twins, however, only the index case is considered as propositus, since the twins are genetically different and can be considered as ordinary siblings. The co-twins

TABLE 3.—*Relationships of Twins Investigated*

	Investigated	Responded	% Responded
Parents	62	62	100.00
Siblings	204	182	89.21
Children	57	49	85.96
First cousins	663	519	78.28
Nephews and nieces	126	109	86.50
Totals	1112	921	82.82

of dizygotic propositi have, therefore, been counted as siblings.

To date, we have investigated 1112 living relatives over the age of 15, and we had the cooperation of 921 of them, or 82.82%. A breakdown of the various relationships investigated and their response are given in Table 3.

The medical records of the 106 relatives who reported neurologic abnormalities were thoroughly searched. In many of them it was decided that a neurologic examination was warranted. To date, 40 neurologic examinations have been conducted in the relatives, which yielded 11 cases of definite multiple sclerosis and 7 cases of possible multiple sclerosis. Many more neurologic examinations remain to be completed. The occurrence of multiple sclerosis among the relatives as of the date of writing is given in Table 4.

The incidence of multiple sclerosis among the relatives of our twins should now be compared with the incidence of the disease in the general population and with that found in other genetic studies. The comparison is made in Table 5.

TABLE 4.—*Incidence of Multiple Sclerosis Among Relatives*

	Definite M. S.	Possible M. S.	Total
Parents	1	0	1
Ordinary siblings	4	4	8
Fraternal co-twins	1	3	4
Children	1	0	1
First cousins	4	0	4
Total	11	7	18

It is especially to be noted that these 11 cases of definite multiple sclerosis were distributed among 9 families; that is, 16.67% of the 54 families of this report were found to have a positive family history.

Comment

It is admitted that the results of our study do not constitute as yet conclusive evidence that genetic factors operate in multiple sclerosis. But before final decision on this point is made, certain considerations are worthy of note. It is obvious that the figures are lessened by several important limiting factors in this study.

1. *Bias of the Original Sample.*—It appears to us that twins concordant for multiple sclerosis may have been lost to our original sample because, since that disease is not considered to be genetic by the generality of the medical profession, it would therefore be rejected in favor of some other diagnosis, such as spinocerebellar degeneration, when a pair of affected twins was encountered. We have no way of estimating

TABLE 5.—*Incidence of Multiple Sclerosis in Twin Relationships and in Other Studies*

	Our Data					
	Incidence	Per Cent	Times Population Prevalence 1:2000	Pratt et al.[9]	Müller[10]	Allison and Millar[11]
Parents	1:62	1.6	32.26	1:200	1:300	
Siblings	1:41 to 1:17	2.44 to 5.88	48.8 to 117.6	1:100	1:100	1:100
Children	1:57	1.75	35.0			
Cousins	1:166	0.6	12.0			
Total	1:101 to 1:61	1.0 to 1.64	20.0 to 33.0			
Family history	9	16.67		6.5	3.6	6.6

this factor in excluding concurrent cases from our series, but there seems no doubt that it has had some effect.

2. *Factor of Variable Age of Onset of Multiple Sclerosis.*—Considering the fact that multiple sclerosis may begin at any age up to 50 years, and even later, it must be evident that many of the as yet free twinmates of our sclerotic probands may still develop the disease. The partial syndrome presented by so many in our series will probably flower into the full clinical picture in many of them, while others now quite free may come to show the full-blown disease. A simple calculation of the past cumulative risk for the development of multiple sclerosis, when projected against the age distribution of our sample, suggests that if multiple sclerosis were 100% genetic in origin, we could expect only 50% concordance at the time of our study, even with full penetrance. But it is obvious that if genetic factors operate in multiple sclerosis, they do not show complete penetrance. We would, then, expect less than 50% concordance—perhaps half of that, or less. Since the concordance rate in our twin cases ranges from 7% to 24% (depending on the rigidity of diagnostic standards), with a true rate falling somewhere between these figures, it can be seen that this true rate would not be far removed from the expected rate. Approximation of the true, discovered rate of concordance and the expected rate would constitute positive evidence for genetic factors in multiple sclerosis.

3. *Factor of Multiple Etiologic Agents.*—Since it seems most unlikely that multiple sclerosis is of purely genetic origin, there must be more than one cause if genetic factors play any role at all. Thus it is possible that a genetic factor may require in addition the operation of an environmental agent before the disease can develop. Concordance in monozygotic twins may thus fail to develop, though both members of the twinship possess the genotype, because one of the pair has not yet encountered the unknown environmental factor necessary to produce the phenotype.

4. *Factor of Diagnostic Difficulty.*—The diagnostic problem has bedeviled all studies on the prevalence and familial occurrence of multiple sclerosis. We have seen how concordance is full in only a few twinships, and how one member of the twinship may show indisputable sclerosis but the other only scattered abnormalities consistent with the diagnosis but inadequate for a positive diagnosis. Again, two monozygotic twin pairs were fully concordant, the twins being equally affected, but both presenting only pyramidal-tract disease with transient sensory changes or nystagmus, so that one can neither establish the diagnosis nor exclude it. Every experienced neurologist has seen such cases, in which the disease finally progressed to the full picture of multiple sclerosis or, on the other hand, proved eventually to be amyotrophic lateral sclerosis or some other disease. We have no way to resolve this difficulty except by waiting for the final developments. At the present time, we segregate such cases and present the facts for the judgment of all.

5. *Factor of "Abortive Multiple Sclerosis."*—Even waiting may not answer the question in some instances (except by autopsy), since we are convinced that multiple sclerosis not infrequently may "burn out," even before the diagnostic features are convincing. Rucker has shown that only 50% of cases of optic and retrobulbar neuritis in young people come to exhibit multiple sclerosis. Certainly, some of the more fortunate 50% represent arrested or abortive cases of that disease. In other patients, we have seen a more complete clinical picture remit to an undiagnosable minimum of abnormalities and remain so for many years. This process in some of our patients may have prevented our establishing a clear diagnosis, and have served to reduce the percentage of concordance among our twins and the frequency of occurrence among relatives.

Our conservative figures must, therefore, be regarded as minimal. Because of most scrupulous care not to make the diagnosis without warrant (an obvious obligation which could not be forsworn) we have underestimated both concordance among twins and prevalence among relatives by an amount which cannot be accurately estimated. For this reason, the comparison of the degree of concordance among monozygotic twins with that among dizygotic twins is not reliable in appraising the genetic factor, because the "limiting factors" operate to an unknown degree in both types of twinship.

The results from the study of the relatives are more convincing. The incidence of multiple sclerosis in the over-all relatives of our twin cases, as well as in the various groups of relatives taken separately, and the incidence of a positive family history are more than double the incidences reported by previous investigators. A preliminary analysis of this material suggests very strongly that a definite genetic factor is operating. For example, a comparison of the ratio of affected siblings to affected cousins points toward a definite mode of inheritance with reduced penetrance. It will not be wise now to go further with the discussion on this point, especially since most of the relatives yet to be examined are cousins.

The facts remain that we have a concordance rate in monozygotic twins which is somewhat comparable to a calculated expected rate; a positive family history in 16.67% of our cases, and a prevalence of multiple sclerosis in the relatives of our twin cases ranging from 20 to 33 times that found in the general population, whereas among siblings of our twin cases definite multiple sclerosis is nearly 50 times as common as in the general population.

This excessive prevalence of multiple sclerosis among the close relatives of our twins is most striking and seems to establish beyond question that multiple sclerosis occurs more frequently among the relatives of patients with that disease than among the general population—a finding already reported by many others. In this sense the equivocal genetic evidence disclosed in the study of twins is made less equivocal—i. e., more favorable to the genetic hypothesis—by the study of the relatives. Follow-up studies of these twins and their relatives, planned for 5 and 10 years from now, will either confirm our predictions or modify our conclusions to more final ones.

Summary and Conclusions

Careful neurologic study of 29 pairs of proved monozygotic twinships with definite multiple sclerosis in one member reveals full concordance in only 2 pairs, while similar study of 25 pairs of proved dizygotic twinships reveals full concordance in only one pair, by the most rigid of diagnostic standards.

Diagnostic standards sufficiently liberal to accept neurologic abnormalities consistent with but inadequate for the diagnosis of multiple sclerosis suggest concordance in 7 out of 29 monozygotic pairs and in 4 out of 25 dizygotic pairs of twins.

A total of 1112 relatives of these twins have been surveyed and 106 found with neurologic complaints. Of these latter, 40 have been carefully studied neurologically and 11 cases of definite multiple sclerosis and 7 of possible multiple sclerosis found. Completion of these studies can only add to the percentage affected, and cannot diminish these figures.

Five factors are discussed, including the bias of our original sample, the variable age of onset of multiple sclerosis, the probably multiple etiologic factors in the cause of this disease, the clinical diagnostic difficulty, and the possibility of an abortive or arrested state in multiple sclerosis, which all tend to reduce our findings of concordance among twins and of prevalence among relatives of the twins.

Our study of twins with multiple sclerosis reveals too small concordance to prove definitely the operation of a genetic factor,

but, similarly, it leaves a genetic factor as a distinct possibility.

Our study of the relatives of our twins demonstrates what has been shown often before, that multiple sclerosis is much commoner among the relatives of patients with that disease than in the general population. This finding strongly suggests a genetic factor as one agent in the causation of multiple sclerosis, but the mode of inheritance cannot be postulated at this time.

8. S. Michigan Ave. (3).

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Regional Differences in Seizure Susceptibility in Cat Cortex

JOHN GARNER, B.A., and JOHN D. FRENCH, M.D., Los Angeles

In recent years the problem of epilepsy has been examined with intensified interest in the experimental laboratory. One technique that has been employed is the initiation of after-discharge by direct stimulation of a cortical locus or nuclear mass in the brain. As this procedure is one which has been utilized clinically,[9,10] experimental data derived from its use would seem to be unusually applicable to the problem of seizures in man.

It was found in a previous study that different regions in the monkey cortex varied in the capacity to exhibit after-discharge when stimulated.[6] These observations indicated that a portion of the motor cortex was the most epileptogenic region on the hemisphere and that this locus responded to low-voltage stimulation by initiating diffuse seizures. Studies in the cat, however, revealed that the motor cortex was far less excitable than in the monkey,[1] it being impossible, occasionally, to elicit a seizure, even locally, by direct stimulation. In order to examine the matter more completely, therefore, it was felt desirable to test the relative excitability of at least the major portion of the convexity of the cat brain to determine whether other zones were more epileptogenic than the motor cortex.

Methods

These experiments performed upon 10 cats were essentially identical in all cases except for minor variations in electrode placement and in craniectomy location. The cortex was exposed bilaterally, small amounts of procaine being injected into exposure margin and pressure areas, and subcortical electrodes placed stereotaxically while the animals were under ether anesthesia. Tracheotomy was made, and the cats were then immobilized with gallamine (Flaxedil), respirations being maintained artificially.

In six of the animals bipolar concentric needle electrodes were placed stereotaxically into the centrum medianum of the thalamus and into the reticular formation of the brain stem. The location of the electrodes was determined at the conclusion of experiments by examination of serial sections stained with thionine. Bipolar silver-ball electrodes were used for cortical stimulation and recording. One recording pair was placed within 2 mm. of the stimulating electrodes to monitor the local response. Cortical recording sites were selected on the ipsi- and contralateral cortical surfaces in such a manner as to make sampling comparable in different animals. Records were made from as many as possible of the cortical loci indicated in Figures 1 and 2 after each stimulus. Usually the stimulus was repeated after an appropriate interval so that tracings could be made from additional unsampled zones. In this manner it was possible to judge activity at a stimulus site and observe its tendency to spread to adjacent or distant loci.

Recording was made by means of a Grass Model III electroencephalograph. Rectangular pulses (240 cps, 2σ, 3 seconds), delivered through an isolation unit from a Grass stimulator, were successively applied to each cortical point to be examined. In testing each point, 5 volts was applied initially. If no discharge occurred, the voltage was raised to 10 and, if the animal was still unresponsive, to 15, or occasionally even higher. Whenever a significant response was elicited at a low voltage, higher voltage was not applied, in order to avoid excessive cortical exhaustion. Stimuli stronger than 15 volts were used only in isolated instances at the termination of an experiment. In order that a reasonable constancy of experimental conditions could be maintained, the intervals between stimuli were arbitrarily selected on the basis of return of the EEG to a prestimulus state.

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From the Veterans' Administration Hospital, Long Beach, Calif., and the University of California School of Medicine at Los Angeles.

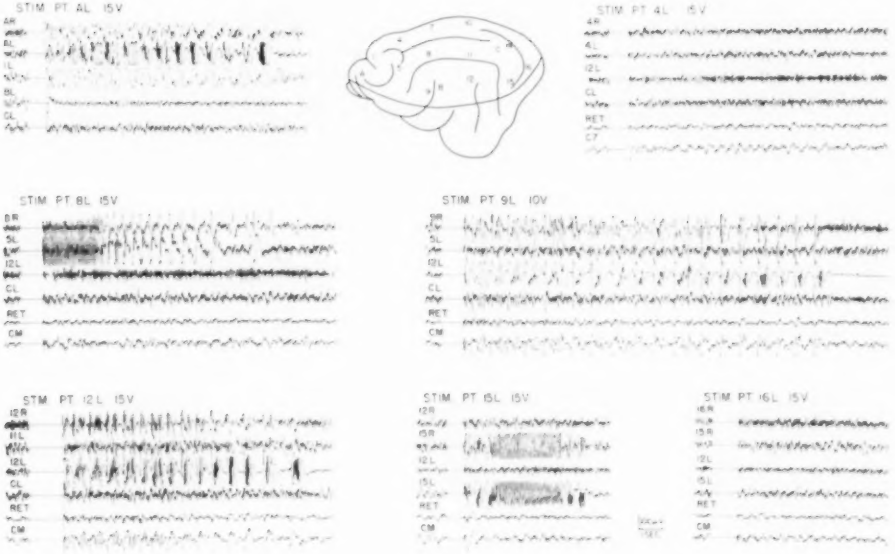

Fig. 1.—The numbers and letters on the diagram of the cat brain indicate stimulating and recording points examined in the experiments. Stimulus is indicated by straight line interposed near the beginning of the records. Note diffuse after-discharge which follows excitation of Points 9 and 12. Craniectomy exposure in all figures was limited to cortex above continuous curved line. Abbreviations in this Figure and in Figure 2: *L* and *R*, left and right hemispheres; *CL*, nucleus centralis lateralis of the thalamus; *CM*, centrum medianum; *RET*, reticular formation; *STIM. PT.*, stimulation point; *V*, volts.

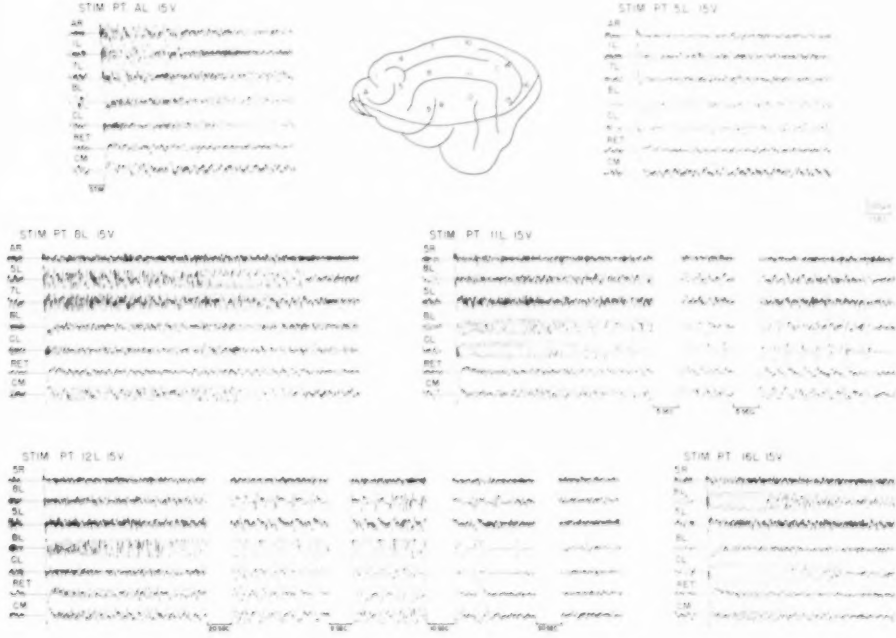

Fig. 2.—The diagram and EEG records are similar to those described in Figure 1. Note prolonged diffuse seizures resulting from stimulation of *Pt. 11* and *Pt. 12*.

Results

By contrast with previous experiments on monkeys,[6] the cat brain was found to be relatively refractory to stimulation, and after-discharge occurred only after the cortical application of much higher voltages, if, indeed, it occurred at all. As the threshold for seizure induction varied so much in the cat, it was found advisable to rate the excitability of different cortical loci in each individual animal, noting most responsive zones, as well as less active loci. In assessing results of each experiment, the cortical areas tested were divided into four groups, ranked according to intensity of after-discharge which resulted from stimuli of graded intensity. Responding loci classified in Group A were characterized by greatest susceptibility, the induced discharge occurring at lowest threshold, lasting longest, and displaying greatest dissemination. Contrastingly, Group D zones required intense stimuli, and any induced after-discharge was very abbreviated. In this group were included loci which never exhibited after-discharge, even after the application of excessively strong stimulation. Between these two extremes, Grades B and C were assigned, respectively, to loci exhibiting after-discharge of intermediate characteristics. Having rated the relative responsiveness of different cortical loci in each cat, it was possible to compare the location of stimulus sites representing Groups A, B, C, and D in all animals (Fig. 3).

Seven cats responded with significant after-discharge during the application of a stimulus within the 5-15 volt range. The other three required stimuli with minimal thresholds in excess of this voltage, although, in these subjects, a representative pattern of response was elicited which was comparable to that seen in other animals which received stimulation of lower intensity. In all experiments, the intensity of after-discharge exhibited by a stimulated area was found to correlate directly with its threshold. Thus, an area which responded more in-

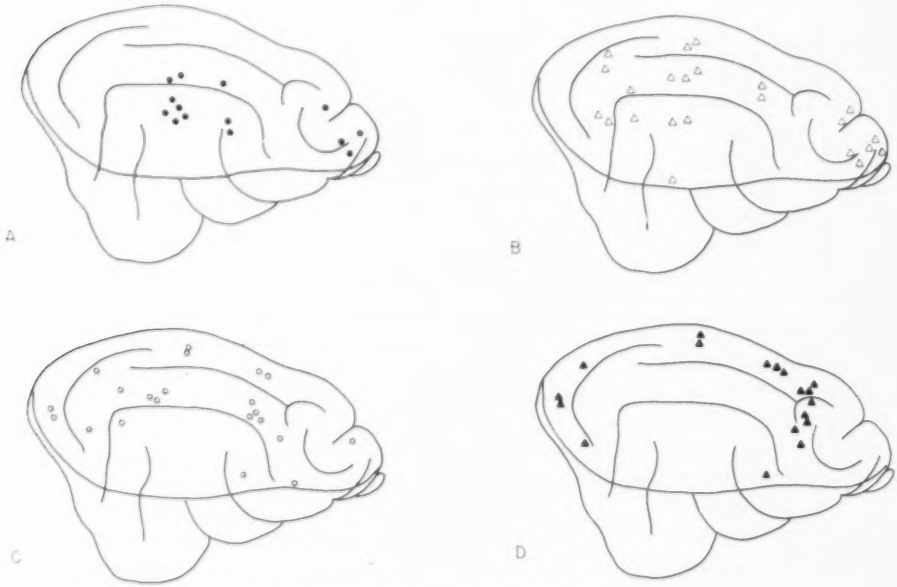

Fig. 3.—Marks on diagrams of the cat brain represent points stimulation of which elicited seizure discharge. Filled circles in *A* indicate most highly epileptogenic loci, while filled triangles in *D* designate least excitable zones. Diagrams *B* and *C* show points from which seizure responses of intermediate intensity were induced.

tensely than a neighboring area to the same stimulus voltage also displayed after-discharge at the lower voltage of the two zones.

General Regional Differences in Excitability

As indicated by the EEG's in Figure 1, the middle sylvian, middle ectosylvian, middle suprasylvian, and anterior ectosylvian gyri comprised the area which in the cat was most susceptible to seizure induction (Fig. 1, *Stim. Pt. 9, Pt. 12*) (Fig. 2, *Stim. Pt. 11, Pt. 12*). While this entire region was relatively susceptible to after-discharge, there was an area, approximately 1.0×1.0 cm. square, which was regularly more epileptogenic than any other portion of the cortex (Fig. 3A). This point of greatest susceptibility varied only slightly in location from cat to cat, and nearly always resided in the region formed by connection of Points *12*, *11*, and *9* in Figure 1. Deep structures from which records were taken were readily fired from these active cortical loci.

Regions somewhat less epileptogenic than those just described, and classified as the *B* areas, were found to be located in the anterior sigmoid, the posterior ectosylvian, the anterior suprasylvian gyrii, a portion of the suprasylvian gyrus, and a small strip of cortex posterior to the cruciate sulcus (Fig. 3*B*). The seizures elicited by excitation of most of these areas were comparable, except for being less prolonged, diffuse, and intense, to those excited from the most sensitive zones (Fig. 2, *Stim. Pt. 8*). The motor area was included in this group in spite of the fact that occasionally it responded to excitation by exhibiting long-lasting, strong seizures locally and in the homotopic point on the contralateral hemisphere (Fig. 1, *Stim. Pt. AL*). The deep structures usually were fired less vigorously, if at all, and seizure activity was not initiated in more remote ipsilateral cortical areas. Moreover, occasionally firing from some points in this region was poorly developed (Fig. 2, *Stim. Pt. AL*).

The still less excitable *C* areas were found in the posterior suprasylvian gyrus and in portions of the lateral and coronal gyri (Fig. 3*C*). These areas responded to stimulation with brief local after-discharge, which occasionally spread to neighboring gyri (Fig. 1, *Stim. Pt. 8*) or to the homotopic zone contralaterally (Fig. 1, *Stim. Pt. 15*), but propagated activity to more remote regions or to the brain stem was never seen at the voltages used in this study.

The least excitable areas, classified as *D*, occupied a strip of cortex extending from the anterior portion of the lateral gyrus to the superior segment of the coronal gyrus around the posterior margin of the coronal sulcus (Fig. 3*D*). A portion of the occipital pole is also included in cortical regions exhibiting comparably low excitability (Fig. 1, *Stim. Pt. 16*). In an occasional animal, a local after-discharge could be elicited from these areas. In most instances, however, stimuli 20 volts above normal intensities commonly employed in other areas were incapable of eliciting any response whatsoever from this zone.

Ipsilateral cortical spread of after-discharge induced by excitation of points in the more active zones commonly was quite generalized but varied somewhat in the intensity with which it affected remote regions. In general, the degree of seizure activity displayed by a locus to which spread had occurred was directly proportional to the excitability of that same region to direct stimulation. Thus, areas relatively refractory to discharge by direct excitation were least affected by spread of seizure initiated from other loci. Contrastingly, more epileptogenic zones displayed greater participation in seizure spread.

Of the deep structures tested which were found to be implicated in seizure spread, the centrum medianum was usually most heavily involved, although in some instances the reticular formation or nucleus centralis lateralis displayed the heavier transmitted

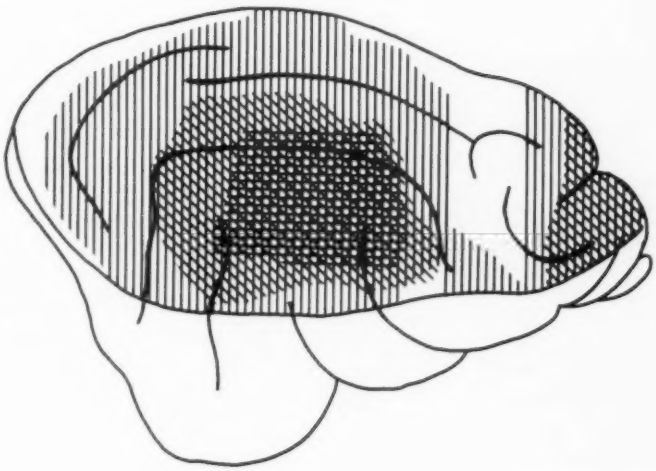

Fig. 4.—This diagram of the cat brain summarizes seizure induction from points indicated in Figure 3. Heaviest hatching represents most epileptogenic cortex, while unhatched zone indicates after-discharge refractoriness.

discharge. No consistent pattern developed from these observations, indicating that a relationship existed between firing in certain cortical loci and a specific subcortical structure.

Contralaterally, the induced seizure remained relatively restricted to the region homotopic to the stimulus site, even when firing was well developed ipsilaterally and in the brain stem. On other occasions, induced firing, which remained very localized ipsilaterally, elicited contralateral homotopic discharge. Thus, regardless of the intensity or dissemination of the seizure, contralateral spread was always very focal.

Comment

The results of this investigation clearly indicate a significant difference between the excitability of the cat cortex and that exhibited by the monkey. In the latter animal lower thresholds were uniformly exhibited, and in no instance did liminal stimulation of an excitable zone fail to elicit a propagated seizure.[6] Contrastingly, 3 of the 10 cats tested in this study failed to display after-discharge when stimulated anywhere on the cortex with maximal voltages.

An additional feature of difference between the two species concerned the location of the most highly excitable region. In the monkey this zone was found to occupy the face-hand-arm region of the motor cortex, while in the cat an area centering in and around the auditory cortex was clearly the most epileptogenic. While the superior temporal gyrus in the monkey, comparable in location to this highly epileptogenic zone in the cat, did exhibit after-discharge upon stimulation,[6] its seizure susceptibility was inferior to that displayed by the motor cortex. In a ratio almost precisely the inverse of that found in monkey, and to about the same degree, the epileptogenesis of the cat sensorimotor cortex was subordinate to the para-auditory region.

While the above differences between the two species were striking, there were similarities in the results obtained in these experiments and those previously reported. In the cat, spread of the seizure from a susceptible zone occurred locally first, and with greatest intensity. Spread to the opposite hemisphere developed early in the process of seizure diffusion, although contralateral extension of discharge always remained quite localized, whereas ipsilateral extension was commonly diffuse. Additionally, as in the monkey, extension of seizure convulsive activity readily occurred to deep midline structures. The centrum medianum of the thalamus was affected strongly in most in-

stances, although occasionally activity in this structure was less intense than was that in the intralaminal thalamic nuclei and reticular formation.

It has been suggested that the nature of the synaptic contacts predominating in different cortical loci contributes to their capacity to initiate a seizure when stimulated.[7,8] This suggestion proposes that the defect in function underlying the initiation and dissemination of after-discharge resides in the dendritic contacts of cells in a nuclear mass. Dendrite depolarization has been found to enhance the excitability of the soma for all-or-none, propagated spike discharge.[4] Axodendritic responses appear to be affected more markedly by seizure discharge than axosomatic ones.[11] Presumably, cortical loci in which axodendritic contacts are functionally most important should be most susceptible to pathological or functional changes which result in after-discharge.

It has been reported by Chang[2] that the termination of collosal fibers arising in a cortical locus on one hemisphere and extending to its counterpart on the other are predominantly axodendritic. In another study, Curtis[5] observed that the most intense homotopic connections existed between the two motor cortices in monkeys. Contrastingly, in the cat, these motor cortical connections are said to be relatively poorly developed,[3] while collosal connections joining the suprasylvian gyrus bilaterally were present in more profusion.[3] It is noteworthy, perhaps, that our maps showing the most highly epileptogenic zones in both monkey[6] and cat (this report) are quite similar to those of Curtis,[5] showing the intensity of cortical collosal connections in both species.

While the relationship between collosal connections and epileptogenesis is striking in general, one bit of conflicting information exists. In Curtis' study[5] the anterior sigmoid gyrus in the cat was represented as having poor collosal connections; yet this region was found to exhibit after-discharge when stimulated. As the after-discharge induced from this locus showed a strong spread to the homotopic area contralaterally, it seems likely that collosal connections are more prominent in this region than they were thought to be. Yet this after-discharge remained quite restricted, never becoming disseminated, as it did uniformly after motor cortex stimulation in the monkey. Clearly, a significant species difference exists in cat and monkey not only in the susceptibility to discharge exhibited by the nervous system of each but in the circuitry through which seizures become disseminated.

It was noteworthy that contralateral seizure spread was limited always to the homotopic point of the stimulated area, whereas homolateral dissemination was often quite diffuse. It follows logically, then, that other ipsilateral loci to which the discharge spread from the zone originally excited to activity were not capable of transmitting the seizure contralaterally. Additionally, the firing focus in the contralateral hemisphere was not sufficiently intense to spread radially, as did the parent discharge. The data available from this study are not conclusive, but they support other observations concerning primary pacemakers. In the normal subject the stimulated locus exhibited the highest degree of postepileptic neuronal exhaustion,[9] and, presumably, when this zone ceased firing, the discharge ceased simultaneously in all leads. All these features point toward the existence of a primary locus (the stimulus site) which drives other areas involved in the after-discharge. The situation may be different, however, when a pathological locus, perhaps a cortical scar, exists. Here, not only are cells in the region of the scar more epileptogenic but connections of these zones with remote areas elsewhere are rendered more susceptible to seizure dissemination.[7] It appears, therefore, that areas having the richest supply of axodendritic associational and commissural interconnections possess the greatest capacity for epileptogenesis.

Summary

The susceptibility of various loci on the cortex to after-discharge elicited by direct stimulation was studied in 10 cats.

1. The middle sylvian and suprasylvian gyri were found to be most epileptogenic, while cortex extending from the lateral gyrus to the occipital pole around the coronal sulcus was relatively unresponsive.

2. Induced seizures spread preferentially to homotopic loci upon the hemisphere opposite the stimulus sites and to central subcortical structures. Most vigorous dissemination resulted from excitation of most epileptogenic cortical loci.

Evidence is reviewed which suggests that axodendritic phenomena contribute importantly to local and diffuse seizure spread.

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Variability of Critical Flicker Fusion Thresholds in Brain-Injured Children

HENRY J. MARK, Sc.D.; PAUL MEIER, Ph.D., Baltimore, and BENJAMIN PASAMANICK, M.D., Columbus, Ohio

This paper reports some differences found between brain-injured (pyramidal-tract-damaged) and control children in critical flicker fusion (CFF) measurements. These results were obtained in the course of studies of intraindividual threshold variability in brain-injured children in various sense modalities presumably unrelated to the area of damage. The investigations were aimed at discovering neuropsychological measurements which might be used to detect otherwise unnoticed alterations in cerebral functioning.

The authors of recent epidemiologic studies [1-6] on the association of maternal and fetal factors with the development of neuropsychiatric disorders have assumed damage to the central nervous system to be the major etiologic agent responsible for reproductive casualties, ranging all the way from abortions and neonatal deaths ("gross" damage) down to behavior disorders and reading disabilities ("minimal" damage). It seems plausible that even minimally damaged persons give altered responses in psychophysical test procedures, and that such responses might be developed into sensitive diagnostic tools for differentiating between central nervous system and psychosocial factors in the etiology of some neuropsychiatric disorders.

Before considering a procedure potentially useful in detecting "minimal brain damage," it should be shown that the procedure either can detect slight damage to the area tested or is sensitive to the effect of a localized lesion some distance from the area tested. By comparing the responses to visual tests of a group of pyramidal-tract-damaged children with those of a group of non-brain-injured handicapped controls of comparable sex, age, and I. Q. distribution, it was hoped to demonstrate the effect of a non-occipital-lobe lesion on occipital lobe functions.

Although CFF thresholds themselves were also of interest, the primary object of study here was the intraindividual variability of the threshold with repeated measurements. It was hypothesized that greater intraindividual variability, rather than the threshold level itself, would distinguish most sharply between the brain-injured subjects and the controls. A marked increase in such intraindividual variability in clinical audiology distinguishes a central hearing and language disorder from an end-organ impairment.[7] Similar findings of increased intraindividual variability in the same subjects as those used here are reported with light perception threshold measurements,[8] as well as with threshold measurements in other sense modalities.[9]

Problem and Hypotheses

In respect to CFF, the psychometric function is a cumulative distribution func-

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From the Departments of Otolaryngology (Dr. Mark) and Biostatistics (Dr. Meier), The Johns Hopkins University School of Medicine, the Department of Psychiatry, Ohio State University College of Medicine (Dr. Pasamanick).

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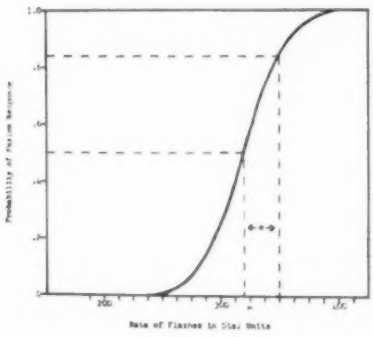

Figure 1

Fig. 1.—Psychometric function: Cumulative normal distribution curve of fusion responses, showing threshold and spread of function.

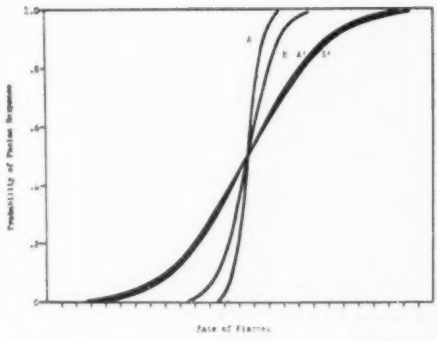

Figure 2

Fig. 2.—Curves *A* and *B* represent the behavior of hypothetical sensory functions having standard deviations of 1 and 2 units, respectively. Curves *A'* and *B'* represent the psychometric functions resulting from the addition of measurement errors having a standard deviation of 5 units to the sensory function values of curves *A* and *B*.

tion (an S-shaped curve) whose value at each flicker frequency is the probability that fusion will be reported (Fig. 1). The threshold point (μ) is conventionally taken as that point at which half the responses are flicker and half are fusion. In these experiments, the estimated threshold is always the mean of a number of threshold measurements. According to our hypothesis, lower thresholds, corresponding to loss of visual efficiency or resolving power, should be associated with the brain-injured. The standard deviation (σ) of the function is a measure of the spread of the curve, i. e., the diffuseness of the threshold. The estimated spread in these experiments is reported as the V-score, and is always taken to be the logarithm * of the variance of the distribution of measurements around the mean, i. e., around the threshold. According to our hypothesis, the brain-injured subjects should show larger V-scores (greater intraindividual variability).

Measurement of spread is complicated by the fact that the observed curve for an individual consists of what is traditionally called a sensory, or "true," component plus a measurement error. Measurement error may include such different sources of variability as subject inattention or clerical error in reading the dials. If this measurement error is large relative to the difference in spread between two subjects, then the resultant large spread due to measurement error will obscure any difference in spread between two subjects which may in fact exist. Thus it can be seen that a technique for distinguishing abnormal spreads (Fig. 2) must not have inherent errors of greater order of magnitude than the spreads of the individual curves.

Subjects.—The brain-injured group was composed of 10 children (6 boys, 4 girls) with diagnosed pyramidal-tract involvement and with no primary diagnosed ophthalmologic pathology. The control group was composed of 10 children (5 boys, 5 girls) with diagnosed conditions which did not justify an assumption of brain damage or injury, such as congenital amputation, clubfoot or Erb's palsy (pseudohypertrophic muscular dystrophy). All subjects attended a Baltimore school for handicapped children. The groups were roughly comparable in terms of age, I. Q., and sex, and the effects of these covariates on all significant discriminators were examined by means of regression diagrams. None of these was significantly related to performance. For example, there was no apparent regression of thresholds or V-scores on I. Q. (which ranged between 64 and 121), and it was therefore assumed that I. Q. did not enter as an important experimental factor in the difference between brain-injured and control groups. The mean I. Q. of the brain-injured group was 89, with a S. D. of 16; the mean for the control group

* The reason for the logarithmic transformation is given in footnote ‡.

was 96, with a S. D. of 16. The age range was from 10 to 15 years, with a mean of 12 for the two groups.

Apparatus.—The apparatus consisted of a Sylvania R 1131C glow-modulator tube mounted centrally on a perimeter so that a focused spot of light could be projected anywhere on the horizontal axis of the perimeter arc by means of a simple achromatic lens. The Sylvania glow-modulator was activated by an electronic pulse-type stimulator and timer, producing a square-wave form.[10] The dial was continuously variable from a setting of 0 to 1000, varying the rectangular pulse of light continuously through a frequency range of 4 to 60 cps. The light-dark ratio was held constant in both experiments at 50% of the cycle, so that each intermittent cycle of illumination was made up of a light pulse equal in duration to the dark period following it. In Experiment 1, a relay was connected to the stimulus unit in order to obtain a 1.2 second electronically timed exposure of the intermittent light by manual operation of a push button. The white focused spot of light was reflected back to the subject by a diamond-shaped piece of white plastic mounted on a background of black velvet cloth. This target subtended a visual angle of 1 degree at a distance of 33 cm. Both experiments were carried out in total darkness. The brightness of the target was of the order of 0.1 mL, as determined with the MacBeth illuminometer. A luminous cross painted on a background of black velvet served as a fixation point for peripheral CFF determinations. A built-in oscilloscope and milliammeter permitted a constant check on the apparatus during experimentation.

Procedure.—In Experiment 1, thresholds were obtained under the following conditions, in the order listed: binocular foveal, right eye peripheral, left eye peripheral, and, again, binocular foveal. The peripheral angle was always 15 degrees nasal.†

Each subject was dark-adapted for five minutes. Duration of exposure of the intermittent light stimulus was held constant at 1.2 seconds, and the subject was asked to indicate whether the light stimulus was steady or flickering. There was a practice period of about five minutes, during which time an attempt was made to demonstrate the physiologic blind spot to ensure proper fixation, and to acquaint the subject with the general instructions. During experimentation instructions were repeated with the presentation of each stimulus, and the subject was encouraged to report fixation failures. Numerous supra- and subthreshold stimuli were interspersed at irregular intervals to ensure alertness and guard against spurious responses. Experimentation was always begun at values well above CFF thresholds and the stimulus magnitude (frequency) decreased in constant steps of 1.24 cps until the subject gave two flicker responses in a five-step range. This was considered the starting point, and a threshold was calculated on the basis of the next 20 responses.

The method of discrete-stimulus presentation employed in Experiment 1 was the up-and-down method,[11] in which the magnitude (cps) of the stimulus to be presented to the subject was determined by the subject's response to the previous stimulus. Thus, if a subject responded "flicker," the frequency of the next stimulus would be increased by a predetermined constant amount; if he responded "steady," the stimulus would be decreased by the same amount.

In Experiment 2, tests were given first for binocular foveal vision and then for left eye peripheral vision (15 degrees nasal). During a five-minute adaptation period the subject practiced reporting flicker and fusion thresholds to a light stimulus of continuously varying flicker rates. The first measurement was always a fusion threshold where a stimulus well below the fusion threshold was presented and the rate of flicker continuously increased at a constant rate of change to the point where the subject reported fusion. This was followed by a flicker threshold measurement obtained in comparable fashion. Five pairs of fusion and flicker threshold measurements were obtained for each of the 10 subjects in the two groups. The fusion threshold was taken as the mean of the five ascending measurements, and the flicker threshold, as the mean of five descending measurements. The V-score was taken as the logarithm of the variance of the five measurements around their mean (i. e., the threshold). This procedure also permitted the calculation of CFF thresholds in the conventional fashion, i. e., by averaging the flicker thresholds and the fusion thresholds.

An additional measure of variability was derived in Experiment 2 by considering the difference, in cycles per second, between the fusion threshold measurement and the flicker threshold measurement of each of the five pairs. In view of the fact that the former was usually greater than the latter, the flicker measurement was always subtracted from the fusion measurement. The mean difference of the five pairs is, of course, equal to the fusion threshold minus the flicker threshold for each subject, and the average fusion-minus-flicker score for the two groups is shown in Table 2. The fusion-minus-flicker V-score in Table 3 was taken as the logarithm of the variance of the distribution of the five differences around the mean difference, i. e., the fusion-minus-flicker score. It reflects a subject's consistency in maintaining whatever

† As this retinal area is thought to contain the largest percentage of cones outside the fovea, it was felt that an interfering rod-cone effect would be held at a minimum.

average difference he chose between fusion and flicker threshold measurements, and is not directly dependent upon either the flicker V-score or the fusion V-score.

Comparisons which might reveal characteristic differences between the groups in thresholds and spreads of CFF functions were made by nonparametric rank methods,[12] which were indicated particularly in view of the sometimes erratic estimates of spread (V-scores) of the psychometric functions. The 5% level of significance was adopted as the criterion for rejecting the null hypothesis of no difference between the groups. This significance level is comparable to the two-tailed 5% significance level customarily adopted.

Results and Comment

Experiment 1.—Threshold scores and V-scores were calculated separately for the first and second foveal measurements. As no major differences between the first and the second measurements were observed, only the mean thresholds and V-scores are reported. Similarly, no differences were observed between the right and left eye peripheral thresholds and V-scores, and here, again, only the mean of each pair of scores is reported (Table 1). Although threshold differences between the two groups were not themselves significant, the change in threshold from foveal to peripheral conditions discriminated between the two groups ($P \leqslant 0.01$). In the brain-injured group the average threshold remained essentially constant (increased by 0.6 cps), but in the control group the average peripheral threshold was 7.6 cps lower than the average foveal threshold. This was contrary to initial expectation, since it was hypothesized that the more difficult peripheral testing conditions would depress the thresholds of the brain-injured more than those of the controls.

Although the average foveal, as well as peripheral, V-scores were higher in the brain-injured group, only the peripheral V-scores were significantly different ($P \leqslant 0.01$) in the two groups. This difference in peripheral V-scores supports the major hypothesis that the brain-injured show increased intraindividual variability.

It is also of interest to note that the brain-injured were significantly more heterogeneous in their thresholds than were the controls (Table 1, † footnote).

Experiment 2.—The average foveal CFF threshold of the brain-injured group was 23.6 cps, while that of the control group was 27.4 cps (Table 2). The difference of 3 cps between the two groups is significant ($P \leqslant 0.01$). The peripheral CFF threshold

TABLE 1.—*Group Averages for the Mean Foveal and Mean Peripheral Scores*

	Brain-Injured		Control		Diff.
	$\bar{X}$	S. D.*	$\bar{X}$	S. D.*	
	Thresholds, in cps				
Foveal	24.3	6.9	27.3	3.3	3.0
Peripheral	24.8	10.1	19.7	3.0	5.1
Foveal minus peripheral	−0.6	5.1	7.6	3.6	7.0 †
	V-Scores				
Foveal	2.85	0.54	2.66	0.64	0.19
Peripheral	3.44	0.69	2.52	0.58	0.92 †

* The F ratio comparing the heterogeneity of brain-injured and control groups is 4.19 for foveal thresholds and 11.36 for peripheral thresholds. The upper 2.5% point of the F distribution for 9 degrees of freedom in both the numerator and the denominator is $F_{.975}(9,9)=4.03$. Thus, foveal as well as peripheral F ratios are shown to be significant at the two-sided 5% level.

† Significant at the 0.01 level.

TABLE 2.—*Average CFF, Flicker, Fusion, Fusion-Minus-Flicker, and Foveal-Minus-Peripheral CFF Thresholds, in Cycles per Second, for the Brain-Injured and the Control Groups of Ten Subjects Each, for Binocular Foveal and for Left-Eye Peripheral Vision*

	Brain-Injured		Control		
	$\bar{X}$	S. D.	$\bar{X}$	S. D.	Diff.
	Binocular Foveal				
CFF	23.6	4.4	27.4	2.2	3.8 *
Flicker	19.5	4.6	25.6	2.5	6.1 *
Fusion	27.7	5.1	29.2	2.2	1.5
Fusion-minus flicker	8.2	4.1	3.6	1.9	4.6 †
	Left-Eye Peripheral				
CFF	19.4	3.5	18.6	1.7	.8
Flicker	13.2	4.8	14.5	3.3	1.3
Fusion	25.6	4.5	22.7	3.0	2.9
Fusion-minus flicker	12.5	6.1	8.2	5.4	4.3
	Foveal-Minus-Peripheral				
CFF	4.2	4.5	8.7	2.0	4.5 *

* Significant at the 0.01 level.

† Significant at the 0.001 level.

difference between the groups was not significant. However, as in Experiment 1, the change in CFF threshold from foveal to peripheral conditions again discriminated between the two groups ($P \leqslant 0.01$), the average CFF threshold of the control group being reduced by 8.7 cps, while that of the brain-injured group was reduced by only 4.2 cps.

As expected, the average fusion threshold was significantly higher in both groups than the average flicker threshold. For the brain-injured group the average foveal fusion-minus-flicker score was 8.2 cps, while the average foveal fusion-minus-flicker score for the control group was 3.6 cps. The difference of 4.6 cps between the two groups in the average foveal fusion-minus-flicker score (which was calculated as an additional index of intraindividual variability) is significant ($P \leqslant 0.001$). It may be of interest to note that the average fusion thresholds were about the same for the two groups, the threshold for the control group of 29.2 cps being 1.5 cps higher than the threshold of 27.7 cps for the brain-injured group. The difference in fusion-minus-flicker scores between the two groups reflects an elevated flicker threshold for the control group, the difference between the groups being 6.1 cps.

TABLE 3.—*Average Flicker, Fusion, and Fusion-Minus-Flicker V-Scores* for the Brain-Injured and the Control Groups of Ten Subjects Each, for Binocular Foveal and for Left-Eye Peripheral Vision*

	Brain-Injured		Control		
	$\overline{X}$	$F_{(\nu_\infty)}$†	$\overline{X}$	$F_{(\nu_\infty)}$†	Diff.
Binocular Foveal					
Flicker	2.70	0.82	2.20	0.89	0.50‡
Fusion	2.72	2.82	2.34	0.93	0.38
Fusion-minus flicker§	3.02	2.35	2.42	1.13	0.60‡
Left-Eye Peripheral					
Flicker	3.11	0.33	2.60	1.97	0.51
Fusion	3.26	4.81	3.04	0.32	0.22
Fusion-minus flicker§	3.42	3.69	2.82	5.76	0.36

* Log variances scores +2.

† If, in fact, all subjects within a group had the same spread, then an F ratio of 1.88 would occur only 1 time in 20.

‡ Significant at 0.01 level.

§ This score is not directly related to flicker or fusion V-scores.

The average V-scores of the brain-injured group are larger than those of the control group (Table 3). Only the average foveal flicker V-score, however, discriminated between the groups at the 0.01 level of significance. (For foveal fusion and for peripheral flicker V-scores, $P<0.10$). This supports the major hypothesis that the brain-injured show greater intraindividual variability. The brain-injured also had a larger average foveal fusion-minus-flicker V-score. This significant difference between the two groups shows that the brain-injured were less consistent in maintaining whatever average distance they chose between consecutive fusion and flicker measurements. The significant F ratio ($F=2.35$), associated with this V-score for the brain-injured, makes this score of particular interest as far as a potential diagnostic indicator is concerned, because it suggests that the technique may be sensitive enough to reflect individual differences within a group. (Significant F ratios ‡ suggest that interindividual variability within a group is greater than would be expected by chance.) The low F values associated with the average flicker V-scores suggest the possibility that within each group subjects had about the same spread, which may thus be considered char-

‡ It will be recalled that the V-score is 2+ the *logarithm* of the variance of the distribution of five threshold measurements in Experiment 2, i. e., $V=2+\log_{10}S^2$ with 4 degrees of freedom (*d. f.*). Now, it is the property of the distribution of such V-scores that their variance will depend *only* on the *d. f.* in the estimate of the V-score.[18] If the psychometric function is a cumulative normal curve, then the variance of $\log_{10}S^2$ with 4 *d. f.* is exactly 0.1216 (if the curve is not a grossly non-normal cumulative curve, this is still approximately true). It is therefore possible to compare the variance obtained for any of the average V-scores in Table 3 with the known constant variance of 0.1216 by the F ratio and establish the significance level. This fact is useful in evaluating the V-score as a diagnostic tool. A large difference between average V-scores suggests that a task may be a good diagnostic discriminator. In addition, a significant F ratio indicates that the interindividual variability within a group is greater than would be expected by chance, and that the task may be sensitive to individual differences within a group.

acteristic for each group. For the foveal fusion-minus-flicker V-score, however, which appears sensitive to individual differences between subjects within one group, the additional possibility exists that the brain-injured could be ranked on a variability scale, which might then be standardized and correlated with other measures or clinical categories.

It is also of interest to note that in general the scores of the brain-injured were less homogeneous than those of the controls, a not unreasonable finding. This is shown in thresholds (Tables 1 and 2), as well as in V-scores (Table 3).

Comment

The critical flicker fusion thresholds themselves did not discriminate as sharply between the brain-injured and the control group as did the light perception thresholds in other experiments with the same groups.[8] The average foveal CFF threshold of the brain-injured group was 3.0 cps lower than that of the control group in Experiment 1, and 3.8 cps lower in Experiment 2, but only the latter difference was significant ($P \leq 0.01$). Although the actual difference between the two groups might be real but not too large, and therefore not always detectable, it may also be that the descending (flicker) threshold measurements are more sensitive to group differences than either the ascending (fusion) measurements or the thresholds obtained by the up-and-down method of Experiment 1.

There are significant differences between the brain-injured and the control group in the magnitude of the reduction of threshold values from foveal to peripheral conditions in both experiments. Such a difference also proved to be the only significant discriminator in a similar experiment using younger subjects and smaller groups. In all three experiments the performance of the brain-injured seemed to "improve" under what was considered more difficult conditions, relative to their own performance under standard foveal conditions. This aspect of the findings was unexpected, and, although there may be a number of explanations, the experiments offer little evidence as to their merit. The phenomenon may be due to more fixation failures in the brain-injured group, thus giving peripheral thresholds contaminated with higher foveal threshold values, or giving higher values due to the fact of the eye movement itself (movement is known to result in higher CFF thresholds). The phenomenon might also be a function of a slightly reduced foveal threshold and a relatively unaltered peripheral threshold in the brain-injured. This possibility could be the result of a larger cortical representation of the fovea, so that the effect of a distant pyramidal tract lesion may be proportionally greater foveally.

Greater intraindividual threshold variability consistently characterized the performance of the brain-injured, thus confirming the major hypothesis of this study. Although the F ratios suggest that some V-scores may be sensitive to individual differences in variability among subjects within the brain-injured group, the findings here are not of immediate practical significance in the diagnosis of pyramidal-tract-damaged children, such as those studied in these experiments. The findings may be considered a step in the direction of developing psychophysical procedures into useful diagnostic tests in that they show variability in visual functions to be a sensitive index of non-occipital-lobe lesions.

A further step would be to apply these techniques to a group which includes subjects with only minimal brain damage. There appears to be no serious difficulty in the epidemiologic selection of such a group. First, an experimental group would be selected on the basis of anamnesis and obstetrical record in which the incidence of all types of brain damage is greater than in a control group selected for lack of pathologic maternal or fetal factors in the history. Subsequent elimination of subjects with demonstrable cerebral pathology from both groups would not affect the incidence

of minimal damage in the two groups. This incidence should still be greater in the experimental than in the control group. If greater intraindividual variability of threshold measurements is again found in the experimental group, then such increased variability may be implicated as one underlying mechanism contributing to the neuropsychiatric disorders found in subjects whose brain damage is not otherwise manifest. Psychophysical procedures may then become useful in identifying some subjects as minimally damaged whose condition had previously been considered essentially in terms of psychosocial etiologic factors. Thus, offering outside validating criteria to establish the likelihood of brain damage, epidemiologic techniques combined with the techniques of neuropsychology may ultimately give us tools of practical diagnostic significance.

Summary

Two experiments are reported comparing the CFF thresholds and intraindividual variability of thresholds of 10 children with pyramidal-tract damage with the thresholds and variability of 10 non-brain-injured handicapped children of comparable sex, age, and I. Q. distribution. Although the foveal CFF thresholds of the brain-injured were lower in both experiments, the difference between the groups was statistically significant only in Experiment 2. The brain-injured had consistently larger V-scores, however, thus confirming the major hypothesis of increased intraindividual threshold variability in the brain-injured. Differential reaction to the more difficult experimental conditions of peripheral (as compared with foveal) testing conditions proved to be one of the best discriminators. The apparent relative "improvement" of the brain-injured under these conditions, however, was contrary to expectation. The potentialities of these findings as diagnostic tools are discussed.

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Regulation of the Cerebral Vessels—New Aspects

HENRY S. FORBES, M.D., Milton, Mass.

In 1954 an interesting paper by Meyer, Fang, and Denny-Brown [1] presented evidence that makes possible a new interpretation of some puzzling features in the response of cerebral arteries to autonomic stimulation.

For the past 20 years there has been general acceptance of the thesis that arteries of the mammalian brain are regulated to a minor extent by vasomotor nerves.[2] The evidence in favor of this is strong. There remain unexplained, however, atypical findings, such as the following: Section of the sympathetic trunk in the neck causes prompt dilatation of cutaneous branches of the external carotid artery, but no dilatation of the pial arteries; sympathetic nerve degeneration (following excision of cervical ganglia) causes increased epinephrine sensitivity of the pupil but not of the pial arteries.

The purpose of the present article is threefold: (1) to illustrate ways in which pial arteries differ from extracranial arteries; (2) to consider a possible alternative to the neural theory of vasomotor control as explanation for the behavior of cerebral arteries, using the paper of Meyer et al. as a starting point; (3) to publish details of two series of experiments performed years ago in our laboratory. Brief mention of these results has previously been made,[2,3] but it seems worth while now to furnish more detail. The first series, by James C. White and myself, shows how in one respect pial arteries do not follow the usual pattern of vasomotor response. The second series, by Nason and myself, shows the effect of stimulating four separate strands of sympathetic fibers.

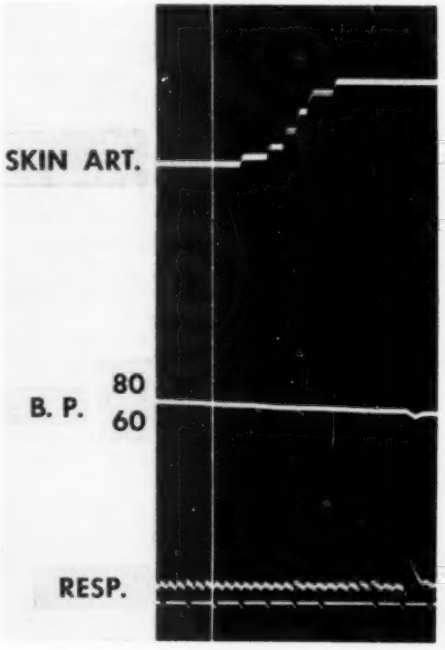
The cerebral arteries certainly act differently, both quantitatively and qualitatively, from those elsewhere in the body.[3] This is illustrated by the accompanying records from our laboratory (Figs. 1-5).

Fig. 1.—Response of an extracranial artery to section of the sympathetic nerve.

A subcutaneous artery of the pinna (left ear) was carefully exposed and flooded with warm Ringer's solution. Over this area a coverglass was placed so that a thin layer of fluid prevented direct contact between the glass and the underlying vessels. A microscope with micrometer scale was placed above the coverglass.

The left cervical sympathetic trunk was cut at the moment indicated by the vertical white line. In five seconds the artery under observation began to dilate strongly. (In contrast to this, we have never —under repeated and careful observation—seen pial arteries dilate under similar circumstances.)

In this Figure and in the following Figures, vasodilation is indicated by an upward movement of the line labeled *Skin Art.* or *Pial Art. B. P.* refers to blood pressure in the femoral artery. In the kymograph records (bottom line) time is recorded at 5-second intervals, with a 10-second pause every minute. All the experiments recorded here were made on cats.



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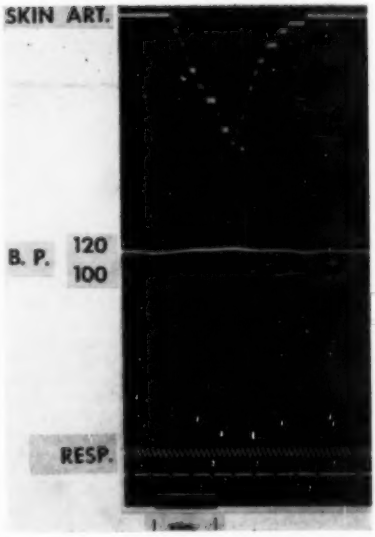


Fig. 2.—Response of an extracranial artery to sympathetic nerve stimulation.

Artery of pinna (right ear). After a latent period of five seconds, the artery constricted strongly on stimulation of the cervical sympathetic nerve trunk on the same side.

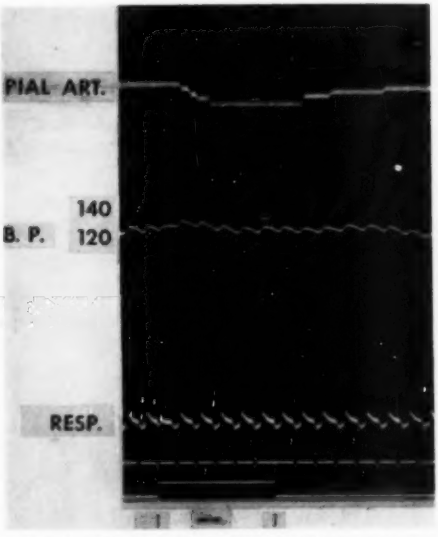


Fig. 3.—Response of a cerebral artery to sympathetic nerve stimulation.

Pial artery (left parietal cortex). After a latent period of eight seconds, the artery constricted moderately on stimulation of the cervical sympathetic nerve trunk on the same side.

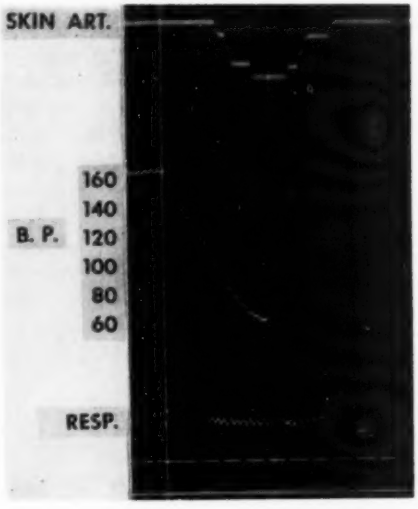
Method

The experimental method used in this work has been described in earlier papers,[4] but here is a brief outline. Through a cranial window sealed tightly and separated from the surface of the brain by a thin layer of fluid, the pial arteries were measured by microscope and ocular micrometer. Strict standards had to be met; otherwise the observations were found to be unreliable. Some of these requirements were maintenance of light general anesthesia and normal blood pressure; avoidance of local trauma, drying, bleeding, fluid leaks, or air bubbles under the window, and elimination of heat from the filament light source by a filter. Changes in arterial diameter were recorded photokymographically in the following way: An observer at the microscope gave measurements, as rapidly as changes could be detected, to an assistant at the kymograph, who at once moved a marker by means of a rack-and-pinion attachment up and down a scale. This traced a white line—"up" indicating dilatation, "down" constriction.

The question still to be answered is this: Are these differences due to a modification of the usual pattern of vasomotor response, or are they due, partly or wholly, to a different mechanism?

Fig. 4.—Response of an extracranial artery to abrupt fall of blood pressure.

A fall in blood pressure (164 to 60 mm.) was produced by manual pressure of the thorax, thus interfering with return of blood to the heart, and with cardiac action. The artery of the pinna (right ear) constricted while the blood pressure was falling, and returned to original size when the blood pressure regained its former level.



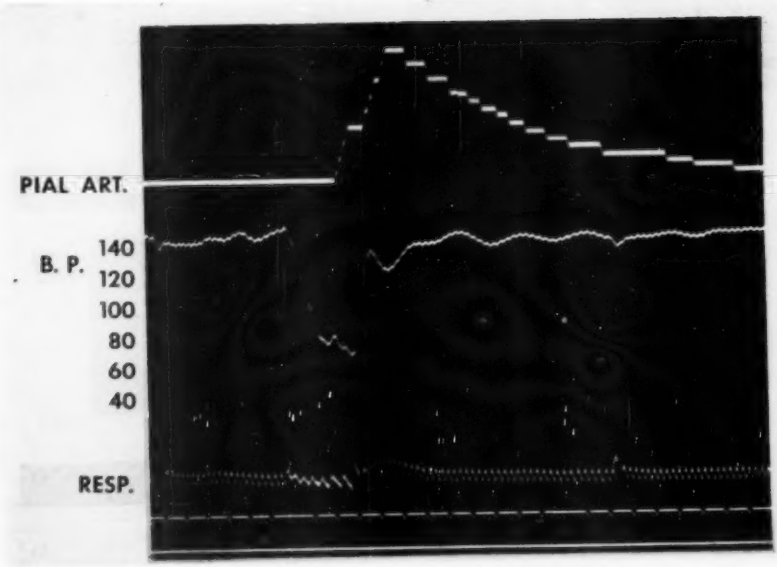


Fig. 5.—Response of a cerebral artery to abrupt fall of blood pressure.

A fall in blood pressure (140 to 66 mm.) was produced by manual compression of the thorax. Pial artery (parietal cortex) dilated sharply when blood pressure reached 76 mm. and was still falling. Seven seconds later, when thoracic pressure was released, the blood pressure rose steeply and the pial artery dilated still further, returning to its original caliber, while the blood pressure remained high.

Several years ago a method of rapid measurement of oxygen concentration was introduced into physiology.[5] Meyer, Fang, and Denny-Brown have obtained important information, using an adaptation of this polarographic method.[1] They measured local changes in tissue oxygenation with multiple platinum electrodes implanted in the cerebral cortex of cats and monkeys. Some of their findings may best be given in their own words:

> We have not seen a significant change in resting cerebral oxygen availability following stimulation or section of the cervical sympathetics in cat or monkey, or following stellate ganglionectomy or section of the facial nerve. We have, however, seen a significant fall in oxygen availability in the temporalis muscle and occasionally an associated rise in cortical oxygen availability following sympathetic stimulation in the monkey, suggesting a shunt from extracranial to intracranial circulation.

In view of this evidence, it now seems possible that some of the phenomena formerly thought to be neurogenic may be due to a change in regional oxygen supply—an adjustment of the cortical circulation to strong vasoconstriction outside the brain. Diversion of oxygenated blood from extracranial regions to the cerebral cortex could cause such narrowing of pial arteries, since a similar degree of constriction has been noted when an animal inhales oxygen. On the other hand, the dilator response following stimulation of the facial nerve might be explained by diversion of blood from brain to salivary and other glands, the pial arteries dilating in response to hypoxia.

Diversion of blood from one source to another undoubtedly occurs when needed, and there is evidence of a delicate balance between demand and supply for widely separated, as well as for adjacent, areas. Occlusion of one or both common carotid arteries will cause a visible increase in flow in the blood vessels of the medulla.[6] Flow is increased not only through the basilar artery but through all the arterial network arising from it,[7] just as a rise in tissue

oxygen of the opposite hemisphere is associated with occlusion of one carotid artery.[1]

Local changes in flow to meet local demands have been shown by various techniques,[8-10] including the cranial window. Under relatively normal conditions the velocity of the red cells passing through the vessels of the pia was remarkably steady. During prolonged observation occasionally one could see red cells in a small venule slow down and even stop and reverse direction of flow for a short time in an anastomotic branch, indicating minute circulatory shifts between adjacent areas of the cortex.[11]

Since widespread, as well as local, shifts in circulation have been observed, it seems quite possible that a readjustment in caliber of pial vessels during stimulation of the sympathetic trunk in the neck might follow as an indirect result of vasoconstriction in the external carotid system. Such readjustments perhaps explain the atypical reactions noted in four experiments by White and myself. Three cats and one monkey were studied. The animals were denervated by removal of the stellate and superior cervical ganglia, and time was allowed for degeneration of the nerves (Figs. 6 and 7). The pupil showed strong sensitization to epinephrine, but the pial arteries showed none.

In spite of the evidence favoring an alternative to the neurogenic theory of vasomotor regulation, some observations are difficult to explain without recourse to it, for example, the decrease in blood flow from the brain, found by Bouckaert and Jourdain when they eliminated completely the extracranial circulation and then stimulated the cervical sympathetic nerve during perfusion of the head. Also, there is our own observation that clamping the external

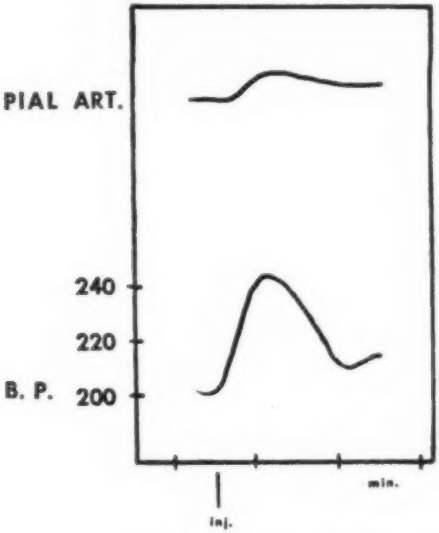


Figure 6

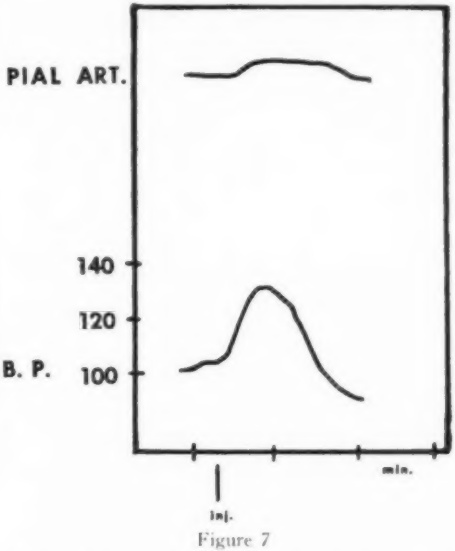


Figure 7

Figs. 6 and 7.—Response of pial arteries to epinephrine.

Fig. 6.—Normal cat. An intravenous injection of epinephrine (0.5 cc. of 1:500,000 solution) is indicated by *inj.*

Fig. 7.—Cat denervated on one side of the head by removal of the left superior cervical ganglion several weeks previously. An intravenous injection of epinephrine (0.5 cc. 1:100,000 solution) is indicated by *inj.*

Pial arteries of the left parietal region were observed in both animals, and no significant difference between the denervated and the normal animal was found. The response in both was a slight vasodilation, but no constriction in either. (A characteristic constriction of an extracranial artery is shown in Figure 8.)

The denervated pupil of the cat in Figure 7 (in contrast to the pial arteries) showed strong sensitization to epinephrine, dilating from 11 to 15 mm. The nondenervated pupil showed no change. In the one monkey, denervated as described, the results were the same as with the cats.

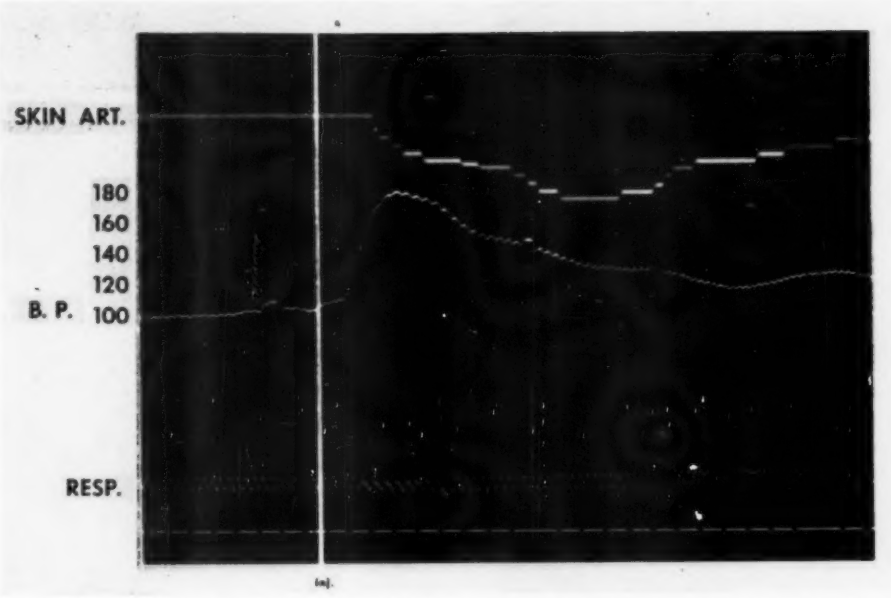


Fig. 8.—Response of an extracranial artery to epinephrine (intravenous injection, 5 cc. 1:100,000). The artery of the pinna (right ear) showed a strong and prolonged constriction, while the blood pressure rose steeply and slowly returned to its former level. (This response contrasted sharply with that shown by cerebral arteries [Figs. 6 and 7].)

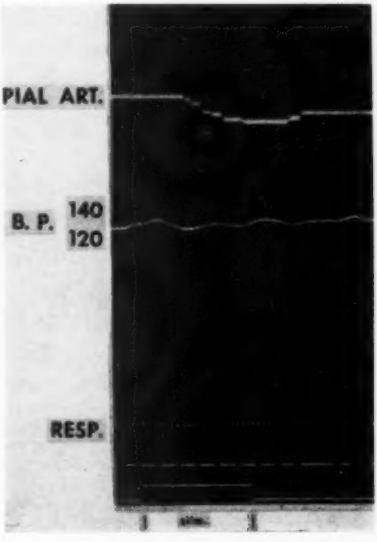
carotid or the common carotid artery causes no change in the response of pial arteries to stimulation of the sympathetic nerve.

Perhaps the strongest evidence for a neurogenic mechanism comes from experiments on sympathetic nerve fibers at the base of the skull. This work was done with Nason, using the same method as that described. The internal carotid prolongation of the sympathetic nerve above the superior cervical ganglion was traced upward by dissection. This necessitated removal of the bulla—a thin shell of bone protecting the inner ear of the cat. Inside the bulla the internal carotid nerve splits up into four strands that pass across the lower surface of the promontory of the cochlea. The result of these experiments is shown in Figures 9, 10, and 11.

In this series 13 cats were used. The operative procedure was difficult, and in seven of the animals the experimental conditions did not meet the standards mentioned earlier in this paper: these experiments were

Fig. 9.—Response of pial artery to sympathetic nerve stimulation; control.

Stimulation of sympathetic trunk while all of the internal carotid nerve fibers were still intact. The four strands of fibers of this nerve were exposed but not cut. The pial artery constricted.



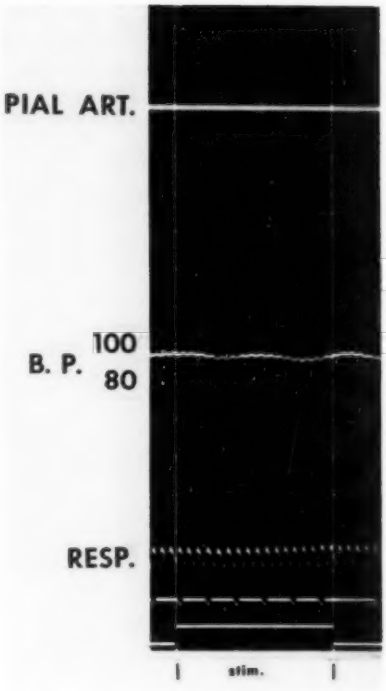


Figure 10

Fig. 10.—Response after cutting fourth strand of fibers.

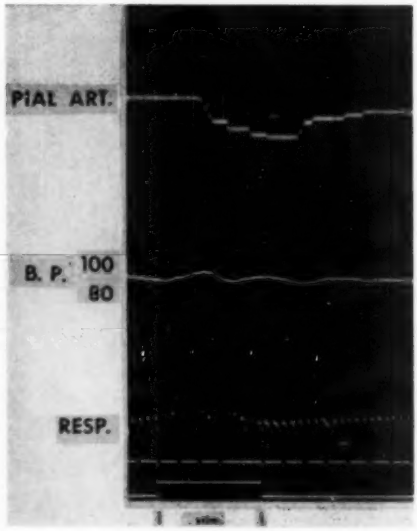


Figure 11

Stimulation of cervical sympathetic trunk after the fourth, or lowest, strand of fibers was cut. The pial artery did not constrict.

Fig. 11.—Response to stimulation of fourth strand of fibers.

Stimulation of the lowest strand of fibers of the internal carotid nerve distal to the point where it was cut. Result: constriction of the pial artery similar to that observed when the sympathetic trunk was stimulated before cutting the lowest strand.

discarded. In the remaining six the conditions were satisfactory and the results clear-cut. Stimulation of the cervical sympathetic trunk was accompanied by constriction of the pial arteries in all six experiments. The result was unchanged after cutting the upper three strands; but when the fourth strand was cut, no constriction occurred. Stimulation of the fourth strand distal to the point where it was cut caused constriction of the same character as that seen earlier when all the fibers were intact.

Dilator fibers of the pupil appeared to be present in the fourth strand in four trials, and possibly also in the third strand in two others. This may have been due to spread of current to the fourth strand. In these experiments on cats it is difficult to see how the external carotid artery, or indeed any extracranial structure, could have been involved.

Summary

Vasomotor nerves seem to exercise a limited control over some cerebral arteries—those on the pial surface of cats and monkeys.

Qualitative and quantitative differences between cerebral and extracerebral arteries are found. Illustrations of these are given, and details from two series of experiments are presented.

An alternative to the neural theory of vasomotor control is suggested, and the evidence for and against this theory is considered.

71 Forest St. (86).

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Cerebral Edema and Electroencephalographic Changes After Local Acute Closed Cerebral Injury

RAYMOND A. CLASEN, M.D.; PAULINE M. COOKE, M.D.; FELIX A. MARTIN, M.D.; JAMES R. WILLIAMS, M.D., and GEORGE M. HASS, M.D., Chicago

Introduction

Changes in the electrical activity[1-7] and water content of the brain[8-10] following experimental cerebral injury have been the subject of extensive study. However, most methods used in production of closed lesions have not permitted accurate definition of either the site or the extent of the damage. Investigators, therefore, could not be certain that the observed changes were due entirely to a local lesion. If, on the other hand, the skull was opened to permit selective placement of the lesion,[11,12] the undesirable and variable effects of surgical exposure of the brain ordinarily interfered with interpretation of the results. These effects were particularly troublesome in a study of cerebral edema, since circulatory and osmotic changes in the brain due to surgical trauma incidental to craniotomy could not be distinguished quantitatively from the changes due to the experimental lesion itself.[13,14]

In order to avoid difficulties incidental to operative exposure of the brain and to eliminate diffuse effects that follow a blow to the head, we have examined changes in electrical activity and water content of the brain following local cerebral injury produced by freezing the brain through the intact skull.

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From the Rush Departments of Pathology, Psychiatry and Surgery, Presbyterian-St. Luke's Hospital.

Post-doctoral Research Fellow, Institute of Neurological Diseases and Blindness, U. S. Public Health Service (Dr. Clasen).

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Methods

The following method was used to produce circumscribed lesions in the cerebral cortex and adjacent white matter of 26 adult mongrel dogs.[15] After intravenous anesthesia with pentobarbital sodium, the scalp was incised and reflected to expose the calvaria. A selected area of the left hemisphere of the brain was then frozen through the intact skull by a special apparatus employing isopentane cooled by liquid nitrogen (Fig. 2). The apparatus was first sealed to the external surface of the calvaria with aquarium cement and then rapidly chilled with liquid nitrogen. It was held in position for 5 to 10 minutes. After evacuation it was warmed with isotonic saline and then detached from the skull. The location of the unilateral lesion produced in the cerebrum of each animal used for electroencephalographic studies is shown in Figure 1. The contralateral hemisphere served as the concurrent control.

Cerebrospinal fluid pressures were measured during each experiment by a standard water manometer attached to a spinal needle inserted into the cisterna magna. In some experiments, after the lesion had been produced, attempts were made to alter intracranial pressure by withdrawing cerebrospinal fluid or by intravenous injection of 50 ml. of a solution of dextran.*

Electroencephalograms were taken with a Grass Model III D electroencephalograph in 14 of the 26 experiments. The small-eyed screws, employed as electrodes, were inserted into the calvaria over points corresponding to the frontal, parietal, temporal, anterior temporal, and occipital areas of both hemispheres. In some instances recordings were taken from additional sites. The midoccipital area or, more commonly, the electrically interconnected ear electrodes were used as common referents and grounded. At times scalp-to-scalp derivations were

* The dextran was supplied by Dr. Homer Stavely, of the Commercial Solvents Corporation.

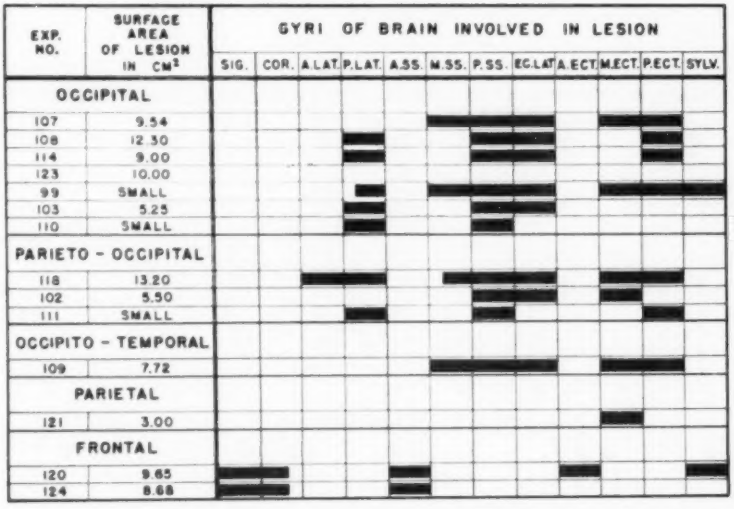


Fig. 1—Surface area of lesions and gyri of brain involved.

also used. Records were taken before, during, and at intervals up to five hours after the production of lesions. Additional pentobarbital sodium was given from time to time to maintain anesthesia.

At the conclusion of each experiment, the animal was killed by an overdose of anesthetic; the skull was opened, and the surface area of the lesion was measured. After the brain was removed, it was weighed and when chemical studies were done, the hemispheres were separated by section of the cerebral peduncles and corpus callosum. Each hemisphere was reweighed after separation from the remainder of the brain. The degree of cerebral damage was estimated in terms of square centimeters of visibly damaged cortical surface per 100 gm. of whole brain.

Chemical studies were done in 15 animals. The water content of each hemisphere was determined by drying in vacuo at 50 C to a constant weight following acetone extraction. The residue and extract were dried separately and then combined for dry ashing with calcium carbonate preparatory to determination of the total iron content of each hemisphere by the *o*-phenanthroline method. The amount of hemorrhage into the damaged hemisphere was estimated by calculating its blood equivalent, in milliliters, from the value of iron in the damaged hemisphere in excess of that in the control hemisphere referred to the amount of iron per milliliter of venous blood. Nonhemoglobin iron was assumed to be equal in the two hemispheres. The calculated water increment due to blood was determined by a method previously described. Details of these procedures are given elsewhere.[16]

Each lesion was classified as early or late, with 180 minutes as the time factor, according to its duration before termination of the experiment. This classification is to be compared with the classification based upon changes in electrical activity, where the time factor was 100-225 minutes.

Results

Description of the Lesions.—Each lesion produced by freezing was sharply circumscribed both externally and on cross section (Figs. 3 and 4). The anatomical distribution of lesions in experiments in which electrical activity was studied is shown in Figure 1. Thalamic nuclei were not directly involved by any deeply penetrating lesion. In some instances, however, the thalamus was encroached upon by the zone of edema which developed around margins of lesions after thawing of the frozen tissues.

In general, the lesions resembled circumscribed areas of contusion or peripheral hemorrhagic infarcts of the cerebrum. Grossly, they were soft and purplish red (Figs. 3, 4). Microscopically, vasodilatation, perivascular hemorrhage, and capillary thrombosis were conspicuous in some areas. In other areas of injury interstitial edema and acute degeneration of neural structure were more prominent (Fig. 5).

Changes in Electrical Activity.—The control electroencephalograms differed greatly among the various animals. For this reason, no attempt was made to compare tracings from one animal with those of another. Instead, each postlesion record was assessed in terms of its departure from the prelesion tracing, which was arbitrarily assumed to be normal for that animal. A decrease in amplitude and in frequency per second of waves and the development of asymmetry between tracings from homologous areas of the control and damaged hemispheres were considered to represent changes in the direction of abnormality, and the reverse, a return toward normal. The spikes and sharp or complex waves, which were occasionally present, were ignored in the present analysis.

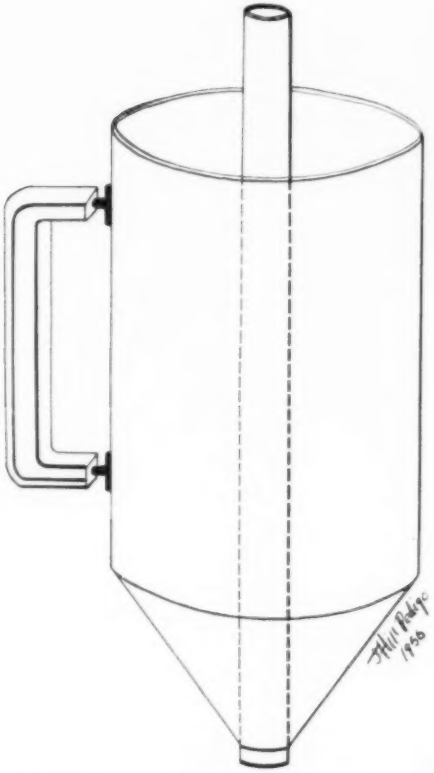


Fig. 2.—Drawing of the apparatus used for the production of lesions. The small axial cylinder is open at both ends. The lower end is sealed against the skull. Isopentane is poured in the upper end; then liquid nitrogen is poured into the large tapered conical cylinder which surrounds the small axial cylinder.

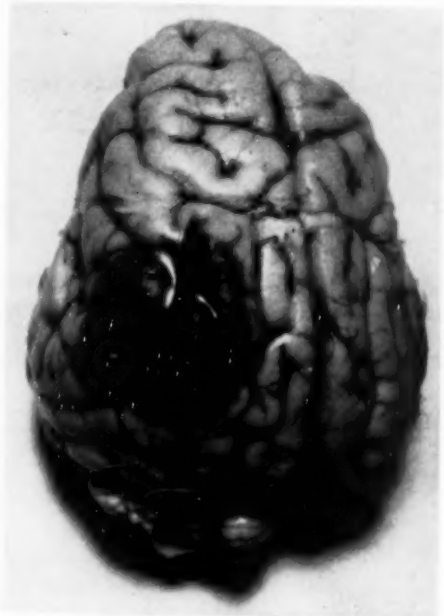
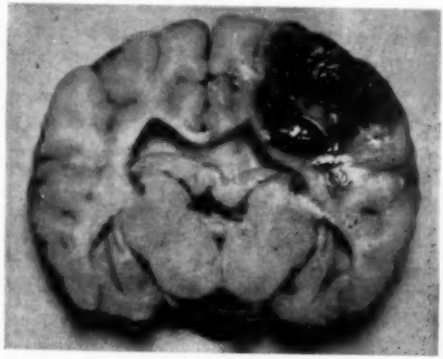


Fig. 3.—Gross external appearance of a typical acute closed hypothermal cerebral lesion. This lesion in the brain was several hours old.

Using these criteria, the records taken before, during, and after production of lesions were compared and the activity remaining in each hemisphere estimated as

Fig. 4.—Coronal section through the lesion shown in Figure 3. The surface area is of average size. No lesion in this series extended deeper into the brain than this one.



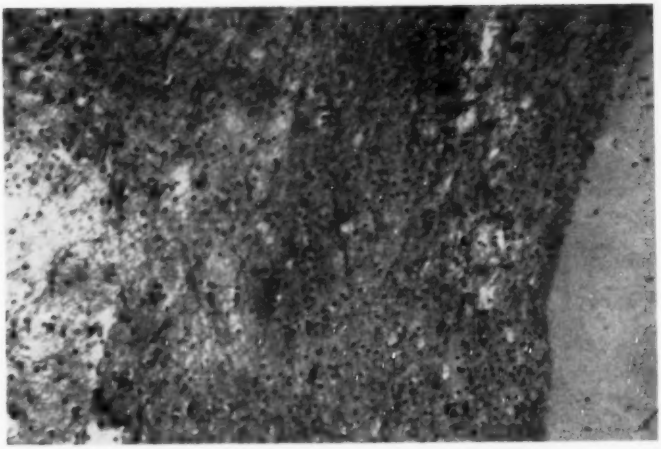


Fig. 5.—Medium-power photomicrograph of a section through the subcortical white matter at the periphery of a lesion of the type shown in Figure 3. The border of the lesion is the massive hemorrhage at the right. Note the patches of poorly stained tissue in which structural elements are more widely separated than normal. Changes of this type were attributed to edema, which was more easily recognized peripheral to the zone of necrosis and hemorrhage than within the lesion itself.

some fraction of the normal. These estimations were quite arbitrary. Each was an opinion of the encephalographer as to how a given portion of the tracing appeared when compared with its control and with immediately preceding sections of the record. These estimations were then plotted on the same diagram with concurrent variations in cisternal pressure as a function of time from the beginning of production of the lesion to termination of the experiment. This was done for each animal,

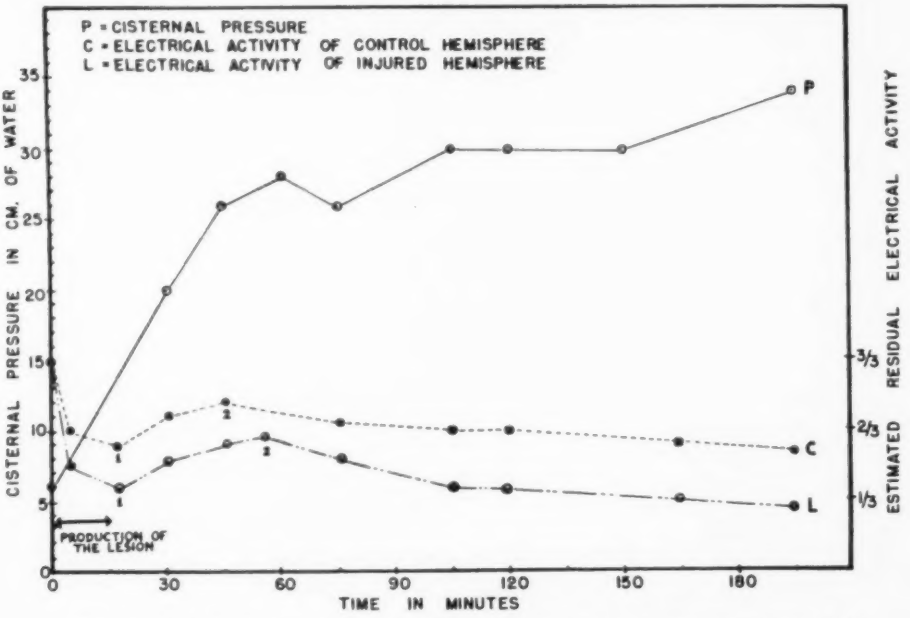


Fig. 6.—A graph of the type illustrated here was constructed for each experiment. This graph pertains to Experiment 120. The changes in the cisternal pressure and the estimated deterioration or recovery of electrical activity of the injured and control hemispheres are plotted against the duration of the lesion, in minutes.

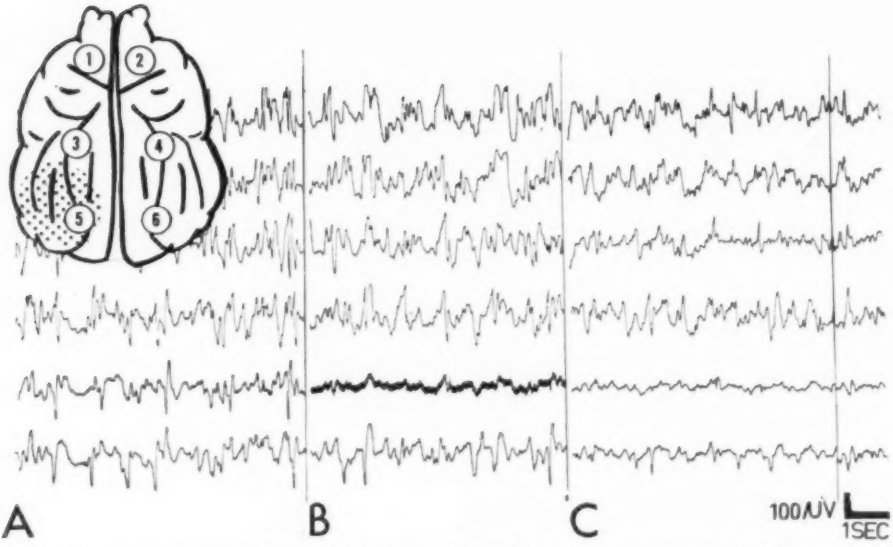


Fig. 7.—Location of a typical lesion in the left occipital area (Experiment 99). Monopolar recording, with both ears as reference, was used. The numbers indicate the channels from the top down (*1* through *6*). The three sections of tracings which are labeled *A*, *B*, and *C* represent electrical activity at different times. The tracing labeled *A* was made just before production of the lesion. The tracing labeled *B* was made during the period in which the lesion was produced. Note the great reduction in electrical activity over the lesion (Channel *5*) and the 60-cycle interference. The tracing labeled *C* was made 95 minutes after the tracing *B*. It represents changes which mark the beginning of the period of secondary decline in electrical activity. All areas show decreased amplitude of waves and a simplification of the electrical pattern generally. There were no subsequent changes in the lesion areas proper.

separately. Figure 6 is an example. In order to make these graphs, the electrical findings were grouped into those alterations noted over the lesion itself, those recorded from other ipsilateral electrodes, and those from points on the contralateral control hemisphere.

During the freezing process, electrical activity at the site of the lesion declined rapidly, until the tracing became very low in amplitude (Fig. 7*B*). Although all frequency bands were affected, the loss at the lesion electrode was greatest for the slowest waves. Quite often during the chilling, 60 cps electrical interference appeared at the electrode nearest the lesion. This disappeared spontaneously as thawing occurred. After thawing there was little or no subsequent change in the tracing from this site (Fig. 7*C*). When the monopolar method of recording was used, any residual activity recorded from the lesion area (Fig. 7*B*,*C*) probably originated at the referent electrode. Under these circumstances it becomes the more active of the pair and may record changes in the potential gradient of brain tissue adjacent to it with respect to the damaged area.

The changes in electrical activity which occurred in other parts of the cerebral cortex followed a similar course in the two hemispheres but were greater on the damaged side (Figs. 7 and 8). These were most obvious immediately adjacent to the damaged zone (Fig. 8*B*, Channels *3* and *5*) and also in the corresponding region of the contralateral, undamaged hemisphere (Fig. 8*B*, Channels *4* and *6*). These electrical alterations consisted of a general decrease in voltage of all frequencies with a relative reduction in prominence of some frequencies, so that the pattern of the tracing became less complex. In this respect the change in pattern resembled that which

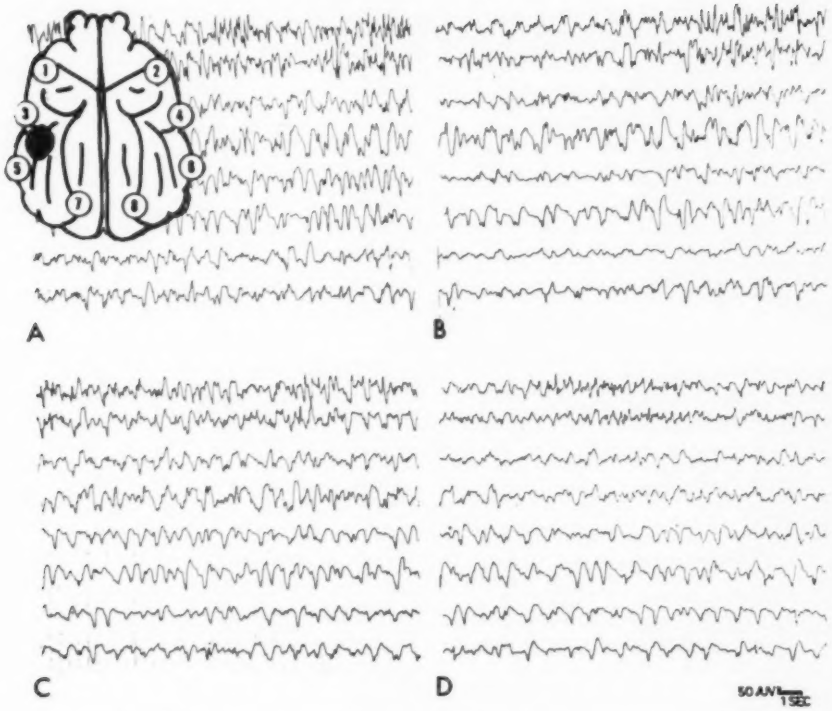


Fig. 8.—Location of a small lesion in the left parietal area (Experiment 121). Monopolar recording with joined ears as reference was used. The numbers indicate the channels from the top down (*1* through *8*). The four sections of tracings, labeled *A*, *B*, *C*, and *D*, represent electrical activity at different times. The tracing labeled *A* was made just before production of the lesion. The tracing labeled *B* represents the period of primary decay immediately after production of the lesion. Note the great reduction in the amplitude of activity in Channels *3*, *5*, and *7* on the side of the lesion. Also, there is relative simplification of the entire record. Attention should also be directed to the prominence of slow waves (frequency 1-2 per second) in Channels *4* and *6* from areas homologous but contralateral to those adjacent to the lesion. The tracing labeled *C* was taken 60 minutes after the tracing *B* and shows changes during the period of improvement following the initial decline. Although there is considerable recovery and the asymmetry is no longer present, slow waves are more conspicuous than in the tracing *A*. The tracing labeled *D* was made 240 minutes after the tracing *B*. It shows the changes occurring during the period of secondary decay. The amplitude of the entire record is reduced, but the tracings from Channel *3* and *5* from areas adjacent to the lesion are reduced more than those from other channels. Note that waves with a frequency of 1-2 per second are dominant in all channels except those from the frontal areas.

follows the administration of a barbiturate anesthetic or which appears at the beginning of asphyxia. Also, the type of change in the pattern of the electrical findings seemed to depend somewhat on the prevailing activity immediately preceding. On the whole, the trends in the records resembled those encountered with increasing depths of anesthesia. Slow activity became more prominent, but was not always greater in amplitude or more synchronous. Bursts that resemble those which follow the administration of pentobarbital sodium often appeared and alternated with periods of relative inactivity, or these latter, if already present, occurred oftener. Occasionally, the first change to accompany the freezing process was a transient increase in the fast activity.

On comparing graphs made by estimating amounts of change in the electrical activity for each experimental animal, several com-

mon features became apparent. The initial process of decay reached an early nadir within or shortly after the period of freezing, but at times required as long as 60 minutes. Occasionally, it appeared earlier on the control curve, indicating that the next stage, one of partial recovery, had begun sooner on that side. The tracings from both hemispheres regularly then returned toward normal but not to the same degree. Their rates varied and regression occurred at times, so that graphs of the activity of the two hemispheres, while similar, were not exactly parallel. At all times the traumatized hemisphere was the more abnormal. There was variation from animal to animal, but recovery was never sufficient to restore even the electrogram of the control hemisphere to its appearance prior to production of the lesion (Figs. 6, 8).

Following this improvement, a secondary period of decay commenced either at once or after a plateau of relative stability. Those patterns which were seen earlier returned; slow waves became more evident, and asymmetries reappeared. Sometimes, spontaneous bursts were absent on the side of the lesion. This change began in both hemispheres within a short time. Appearing first in areas adjacent to the lesion (Fig. 8*D*, Channels *3* and *5*), it spread to other areas of the same side. However, homologous contralateral regions were altered at times even before more distant points on the traumatized cortex. As this change progressed, the electrical activity declined in amplitude until tracings, particularly from areas near the lesion, often consisted of a fairly straight base line with superimposed relatively fast deflections of low amplitude.

Since there was a change in electrical activity in both hemispheres, one may postulate that the change may not be due to the lesion itself but be the result of some more general effect secondary to the lesion. One general effect of this type was in cerebrospinal fluid pressure changes, which occurred during and after production of the lesions. In this connection the series of animals were divisible into two groups with respect to the time at which the secondary decline began. In the early group (four dogs) secondary decline appeared about 45-60 minutes after the start of freezing. The late group (eight dogs) began to show the secondary decline at 100 minutes, or as long as 225 minutes, after the beginning of cerebral freezing. In two experiments the animal could not be placed in either group. There was one instance of an early secondary decline of electrical activity of the traumatized cortex with a late failure of its control and one instance of the reverse. When fluctuations of cerebrospinal fluid pressure were compared with the graphs of estimated electrical activity prepared for each experiment, there was no constant relationship in time between pressure changes and changes in electrical activity. Neither the time of peak pressure nor any particular time interval thereafter could be correlated with the onset of secondary decay of the electrogram. While at times pressure was rising as the tracing became worse, this relationship was not invariable. Likewise, the downhill trend of electrical activity was not reversed by temporary reductions in cisternal pressure following withdrawal of spinal fluid or elevations of pressure following intravenous administration of solutions of dextran. Furthermore, it was not possible to relate the time of onset of secondary decline of the electrogram after freezing with either the location or the size of the lesion, as given in Figure 1.

Relation of Electroencephalographic Changes to Changes in Blood and Water Content of Damaged Hemispheres.—Although the commonly observed rise in cisternal pressure was not directly related to the secondary deterioration of the electroencephalogram, the study of the lesions indicated that local intracerebral bleeding into the lesion with subsequent regional edema, or both, might have a bearing on the secondary decline.

TABLE 1.—*Group A: Chemical Analysis of Canine Brains with Unilateral Lesions Less Than 180 Minutes Old*

Exper. No.	Undamaged Hemisphere: Weight, Gm.	Undamaged Hemisphere: Content, Ml/100 Gm. Blood	Undamaged Hemisphere: Content, Ml/100 Gm. Water	Surface Area of Lesion, Sq. Cm/ 100 Gm.	Damaged Hemisphere Increment, Ml/100 Gm. Blood	Damaged Hemisphere Increment, Ml/100 Gm. Water	Water (Calculated) Due to Blood	Water (Actual) Minus Water (Calculated)
58	31.86	3.52	78.52	4.85	3.30	0.00	0.39	—0.39
61	25.58	4.82	77.97	6.03	1.88	0.11	0.29	—0.18
64	24.29	2.16	—	6.67	0.31	—	—	—
67	23.97	7.73	77.89	10.50	0.02	1.33	0.01	+1.32
113	24.50	6.38	78.75	11.40	3.21	1.29	0.53	+0.76
115	29.52	—	80.22	7.00	—	0.69	—	—
117	27.84	5.42	76.70	12.20	0.08	0.70	0.04	+0.66
x̄	26.79	5.01	78.34	8.38	1.47	0.69	0.25	+0.43
sx̄	1.14	0.81	0.475	1.1	0.63	0.23	0.10	0.31
t *					2.33	3.00		

* Comparison of differences between the damaged and the undamaged hemisphere of the same animal: $t = \frac{\bar{x}}{s\bar{x}}$

The chemical measurements of blood volume and water content of the brains of 15 animals with unilateral lesions are given in Tables 1 and 2. The tabulation lists the weight, blood content, and water content of the undamaged hemisphere, together with the increment of water and blood in the hemisphere containing the lesion. The t-test indicates that these increments are significantly greater than zero at the 5% level of probability.

The animals were divided into two groups according to the age of the lesions. In Group A the lesions were less than three hours old, while in Group B the lesions were more than three hours old. When the

TABLE 2.—*Group B: Chemical Analysis of Canine Brains with Unilateral Lesions More Than 180 Minutes Old*

Exper. No.	Undamaged Hemisphere: Weight, Gm.	Undamaged Hemisphere: Content, Ml/100 Gm. Blood	Undamaged Hemisphere: Content, Ml/100 Gm. Water	Surface Area of Lesion, Sq. Cm/ 100 Gm.	Damaged Hemisphere Increment, Ml/100 Gm. Blood	Damaged Hemisphere Increment, Ml/100 Gm. Water	Water (Calculated) Due to Blood	Water (Actual) Minus Water (Calculated)
59	22.95	6.15	78.09	1.50	3.43	0.21	0.50	—0.29
63	27.80	3.39	79.14	14.40	8.29	1.00	1.14	—0.14
82	23.07	5.67	78.59	12.50	3.71	0.89	0.50	+0.39
91	27.77	4.98	78.97	15.60	2.32	1.01	0.20	+0.81
97	26.83	4.43	78.30	13.30	2.92	1.38	0.50	+0.88
102	29.94	5.34	76.61	7.30	2.87	0.62	0.06	+0.56
103	32.67	4.28	79.25	6.60	0.76	0.88	0.15	+0.73
107	30.86	3.73	79.32	12.00	2.30	1.20	0.37	+0.83
x̄	27.74	4.75	78.53	10.40	3.32	0.90	0.43	0.47
sx̄	1.22	0.338	1.00	1.7	0.77	0.126	0.12	0.16
t *					4.31	7.14		
t †		0.59	0.52	1.16	1.77	0.88		

* Comparison of differences between the damaged and the undamaged hemisphere of the same animal: $t = \frac{\bar{x}}{s\bar{x}}$

† Comparison of means of Group A (Table 1) and Group B: $t = \bar{x}_1 - \bar{x}_2$

$$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\frac{n_1(n_1-1)s\bar{x}_1^2 + n_2(n_2-1)s\bar{x}_2^2\left(\frac{1}{n_1}+\frac{1}{n_2}\right)}{n_1+n_2-2}}}$$

means of the two groups were compared, it was found that they were statistically the same for water and blood content of both injured and uninjured hemispheres. However, when the maximum calculated water increment due to excess blood in the damaged hemisphere (based upon the maximum reported water content of canine blood, 92%) was compared with the measured water increment, the *t*-test performed on the means indicated that the figures were statistically the same at the 5% level of probability for Group A ($t=1.63$). On the other hand, for Group B there was a significant difference at the 5% level of probability between the maximum calculated and measured water increments ($t=2.76$). This indicated that there was significantly more water in the damaged hemisphere than could be accounted for by the measured accumulation of blood in lesions more than three hours old. As previously shown, there was also a direct correlation between the water increment and the degree of damage as determined grossly in the late group.[15] There was, however, no correlation between the amounts of damage and the degree of hemorrhage or between the water and blood increments when they were directly compared.

Our interpretation of these data is that cerebral edema developed progressively over a period of several hours following the production of the lesion. More microscopic and chemical data, including data on the distribution of cerebral electrolytes in more prolonged experiments, are needed to clarify this point. Until these data are obtained, correlations between the secondary decline of the electrograms and the onset of cerebral edema, though suggestive, cannot be regarded as fully established. Nor can the changes in the electrogram of the contralateral, undamaged hemisphere be correlated satisfactorily with the available chemical data.

Comment

Several mechanisms can be advanced to account for the primary and secondary changes in electrical activity of the cerebral cortex when it is subjected to the freezing procedure. Because the evidence is at present insufficient to permit us to decide between them, each will be mentioned. It is hoped that further experiments will limit the choice.

As might be predicted, since the rate of the chemical reactions responsible for electrical activity of the brain depends upon the temperature, the chilled portion of the brain became electrically inactive. The rat's electrogram changes progressively with declining body temperature until at 18 C it becomes a straight line.[16] These alterations were reversible, as were those reported by other authors whose methods of cooling the cortex were less drastic than ours.[17-19] When the isopentane-liquid nitrogen method was used, the area which was frozen became permanently inactive, and in this respect the result was similar to that found after thermocoagulation.[20] Reports of histologic study following use of high temperatures were not given, so that comparison of the hyperthermal lesions with the present hypothermal lesions cannot be made.

The present data indicated that a change in the rate of cerebral electrochemical activity due to a local drop in temperature was not the only reason for the primary decline in activity of the rest of the cortex, even though some reduction in the temperature of the brain at a distance from the site of the lesion doubtless occurred. When the area being chilled was in the upper portion of the convexity of the hemisphere, it might be expected that changes in the electrical activity would diminish with increasing distance from this site, would be greater on the same side, and would be less marked, but uniformly evident, on the other side. This was not always the case. At times there was more alteration in the tracing from a similar area on the contralateral side than appeared in tracings from the same hemisphere at an equal distance from the chilled tissue. Both this distribution and the way in which changes seemed

to progress across the cortex resembled the spreading depression of electrical activity following local injury to the pia and superficial layers of the cortex.[21-23] As far as we know, a spreading depression of electrical activity has not been demonstrated without directly exposing the cortex to air. Nevertheless, heretofore, this mechanism has been considered as a possible explanation for some of the electrical changes following a concussion.[24] If the various patterns of cortical activity seen in the electrogram depend partly upon "tonic influences" from other cortical areas, then the inactivation of many neurons in one area might be expected to change the patterns of regions functionally related to them. Such changes in electrical activity have been recorded at some distance from a place on the cortex subjected to local thermocoagulation.[20] In the hyperthermal experiments the metabolic effect of chilling can be ruled out.

It might also be postulated that the widespread changes accompanying the development of the lesion were due to the effects of an injury potential created by interruption of a large number of incoming axons from related areas. Presumably, this interruption could alter the activity of cell bodies of incoming axons sufficiently to account for the changes in the electroencephalograms.

The effects of the rapid changes in intracranial pressure which accompanied production of the lesion should also be considered. Slow waves have been reported in the presence of increased intracranial pressure in man.[25] This association, however, is inconstant,[26] and when it does occur, there is no direct relationship between the height of the pressure or the degree of papilledema and the frequency of the brain waves.[27] Similarly, in experiments upon the kitten, when the intracranial pressure was acutely or chronically raised, there was no corresponding increase in large slow waves.[28] None of these authors made a distinction between high-amplitude, regular, slow waves and the lower-amplitude, irregular, and much slower fluctuations which appear mainly as an instability of the base line in the conventional electroencephalogram. The improvement which we have noted in the presence of rising intracranial pressures also speaks against this last explanation and to some extent weakens the explanation based upon loss of "tonic influences" from the area of the lesion. An injury potential would be expected to diminish. Subsequent warming of the brain or recovery from the hypothetical spreading depression might also account for the various degrees of recovery before the secondary deterioration began.

The late changes in electrical activity appeared to fall into two groups. Those which developed after the longer interval of about 100-225 minutes may be due to progressive edema, since the chemical studies indicated that edema had become demonstrable by this time. An increase in water content of cerebral tissue has been shown to be associated with progressive changes in the electrogram in the frog[29] and in the rat.[30] In the latter animal, there was first an increase in the higher-amplitude slow activity, and then this was followed by a drop in voltage and fading out of activity as more water was introduced. These changes could be reversed.

The second group was composed of animals in which electrical deterioration began earlier, usually after about 45 minutes. Chemical studies indicated that in this group the increase in water content of the damaged hemisphere was no greater than that which might possibly be ascribed to hemorrhage into the cerebral lesion as it thawed. Yet the electrical changes in the early and late groups did not seem to differ. It is still possible that a local increase in pressure with resulting impairment of the circulation to neurons at the periphery of the lesion is the fundamental disturbance in both groups, but this fails to account for the widespread distribution of the changes and once more raises the problem

of the relationship between the over-all intracranial pressure and electrical activity of the brain. In any event, the observations have disclosed a quantitative topographical means by which attempts to solve the relations between a focal cerebral lesion and homolateral, contralateral, or generalized changes in the electrical activity of the cerebral cortex can be made.

Summary

Circumscribed reproducible acute lesions were made in the cerebral cortex and subjacent white matter of 26 dogs by local freezing of one hemisphere through the intact skull. As the frozen region thawed, it became purplish-red and soft, resembling a hemorrhagic infarct. Within the volume of damage there was vasodilatation, perivascular hemorrhage, and thrombosis of the capillaries, with interstitial edema and acute degeneration of neural structures. Electroencephalographic studies disclosed a series of changes in the electrical activity of the brain during the production and subsequent evolution of the lesions. The frozen tissue became electrically inactive and remained so. Elsewhere, there was a reduction in amplitude of the waves. The wave patterns became simpler and slow activity more conspicuous. These changes were greater ipsilaterally, and more so adjacent to the lesion, so that the tracings became asymmetrical. Parallel, but less pronounced, changes appeared in the tracings from the contralateral, undamaged control hemisphere. After the initial decline in electrical activity, the electrograms of both hemispheres returned toward normal. Then, either immediately or following a plateau interval, secondary deterioration began, and there was a return to the previous patterns and distribution of abnormal electrical activity. In one group of animals this secondary decline began about 45 minutes after freezing was started. In a second group it was delayed for 100 or more minutes. The decline was not correlated with the time at which cisternal pressure reached its peak or with any subsequent interval, and the changes in cisternal pressure and electrical activity did not necessarily run parallel. Neither was there any consistent relation between the time of onset of electrical changes and the location or size of the lesion. Chemical studies disclosed an increase in water and blood in the damaged hemisphere as compared with the undamaged hemisphere. There was more water in the damaged hemisphere of animals killed after 180 minutes than could be accounted for by the measured amount of hemorrhage. This increase in water content was directly correlated with the size of the lesion. There was no correlation between the amount of blood in the damaged hemisphere and either the total water or the size of the lesion. Emphasis is placed upon the possible dependence of the secondary deterioration of electrical activity on the progression of cerebral edema. Possible explanations of the relations between the evolution of the unilateral local acute cerebral lesions and the ipsilateral and contralateral sequence of changes in electrical activity of the brain are discussed. It is concluded that none of them fully accounts for the observed changes.

Presbyterian-St. Luke's Hospital, 1753 W. Congress St. (12) (Dr. Hass).

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Effect of Dysphasia and Spatial Distortion on Wechsler-Bellevue Results

HALLGRIM KLØVE, Cand. Psychol., and RALPH M. REITAN, Ph.D., Indianapolis

Psychological testing of patients with complaints resulting in admission to neurology and neurological surgery services frequently reveals striking deficiencies in fundamental abilities. In a group of 221 patients with verified brain damage, 64 (29%) showed an inability to copy a Greek cross without clear error or distortion. Forty-seven (21%) of the group showed definite evidence of dysphasia. Twenty-one of these patients showed both of these deficits. Since disabilities of these types are usually easily detected and demonstrated without detailed or time-consuming testing, it seemed of value to inquire regarding the possibility of their more general significance with respect to psychological test results.

Material and Methods

In composing the groups for comparative study the first step was to select all patients who gave evidence of dysphasia or who had any difficulty in copying a Greek cross. The Halstead-Wepman Aphasia Screening Test had been administered to each patient routinely and was used for this purpose, since it includes items designed to detect both of the deficits we were considering.

Prior inspection of a sample series had suggested that the reasons for difficulty in copying the cross fell into three categories: (1) distortion of the spatial configuration, (2) poor motor control, and (3) general apraxia. In this study we wished to use those patients whose difficulty was expressed by distortion of the spatial configuration.

We independently sorted attempts to copy the cross from 64 patients into the three categories mentioned above and agreed in 62 of the 64 instances. The only patients used in this study represented instances in which we both had agreed that the difficulty was a failure to effect the proper spatial organization of the cross rather than a failure of motor control or a failure in ability to use a pencil effectively (general apraxia). The only additional reasons for not including certain patients from the original group of 221 were left-handedness or incomplete psychological test results.

Three groups were composed. Group I consisted of 36 patients who had difficulty in effecting the correct spatial configuration when attempting to copy a Greek cross. Group II was composed of 22 patients who showed definite evidence of dysphasia, even though in many cases dysphasia was mild. Group III was composed of 13 patients who demonstrated dysphasic symptoms and, in addition, had difficulty in attempting to copy a Greek cross. The three groups were similar in age and education. Results on these variables, together with others, are presented in Table 1.

Mean Halstead Impairment Indexes were computed for each group, and these failed to show any significant differences in intergroup comparisons. All subjects were right-handed.

The Wechsler-Bellevue Scale of Adult Intelligence (Form I) was administered to each subject and scored completely before any of the groups were composed. No attempt was made in this study to select patients with respect to such variables as localization, extent, or type of brain lesion. While these factors may very possibly have relevance to

Fig. 1.—Attempts of three patients to copy the Greek cross (shown at left) in which the spatial configuration was distorted.

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From the Departments of Neurology and Surgery (Section of Neurological Surgery), Indiana University Medical Center.

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TABLE 1.—*Descriptive Variables for Three Groups of Patients*

	N	Sex	Mean Age, Yr.	S. D.	Range	Mean Education	S. D.	Range
I. Difficulty in copying cross	36	28 M 8 F	43.44	13.91	16-68	9.11	2.72	3-14
II. Dysphasia	22	19 M 3 F	42.36	15.38	17-71	9.18	2.24	6-14
III. Difficulty in copying a cross and dysphasia	13	12 M 1 F	44.77	14.20	19-65	9.31	2.94	5-16

the results obtained, since lateralization, and possibly localization, have some association with the criteria used for composing the groups, the design of the present study is such that it does not permit their evaluation.

Results

Means and standard deviations on Wechsler-Bellevue variables for the three groups are presented in Table 2.

Table 2 indicates that Group I had lower mean values on four of the five performance subtests than on any of the verbal subtests. On the contrary, Group II tended to have lower mean scores on the verbal subtests than on the performance subtests. Group III, in which the patients were dysphasic in addition to having drawn defective crosses, showed no particular difference in level between the verbal and the performance subtests. These results can be summarized by comparing the means for the verbal and performance total weighted scores, with Vocabulary omitted from the verbal total in order to have five subtests contributing to each total. Group I, composed of those patients who had difficulty in effecting the spatial configuration of the cross but with no dysphasia, had a mean verbal weighted score exactly 11 points higher than the mean performanance weighted score. Group II, composed of patients with dysphasia but with no difficulty in copying the cross, had a verbal weighted score exactly 8 points lower than the performance weighted score. In Group III the difference between the mean verbal weighted and performance weighted scores was only 3.85, and each mean fell at approximately the level of the lower mean in Groups I and II. A graphic representation of these results may help to

TABLE 2.—*Means and Standard Deviations of Wechsler-Bellevue Variables for Patients Unable to Copy a Greek Cross (Group I), for Patients with Dysphasia (Group II), and for Patients with Both of These Deficits (Group III)*

	Group I		Group II		Group III	
	Mean	S. D.	Mean	S. D.	Mean	S. D.
Information	8.62	2.22	7.28	3.79	7.07	3.12
Comprehension	8.78	3.38	6.32	3.76	5.84	2.70
Digit Span	5.45	2.95	2.78	2.85	3.61	2.68
Arithmetic	5.48	3.99	4.64	3.77	3.84	3.14
Similarities	7.87	2.87	5.46	3.56	5.45	3.73
Vocabulary	9.17	2.86	5.79	4.05	7.31	3.12
Picture Arrangement	4.64	2.36	6.51	3.43	5.15	3.09
Picture Completion	7.14	3.40	8.19	3.64	5.00	4.19
Block Design	4.23	2.26	7.28	2.59	4.31	3.04
Object Assembly	4.98	3.86	7.46	3.30	4.46	3.65
Digit Symbol	4.11	2.23	5.51	2.26	3.23	2.19
VWS	36.17	11.28	26.45	14.22	25.84	11.28
PWS	25.17	10.75	34.45	11.61	22.00	14.40
Total WS	61.35	17.68	60.97	23.46	47.83	22.80
Verbal IQ	91.16	13.24	79.72	15.97	80.77	11.33
Performance IQ	80.18	13.43	90.36	14.39	78.23	14.88
Full-scale IQ	85.07	12.68	84.22	15.66	77.92	12.95

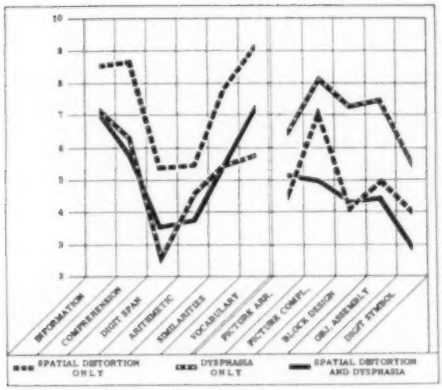

Fig. 2.—Graphic representation of mean results on Wechsler-Bellevue subtests for three groups.

clarify the comparative performance on verbal and performance subtests in the three groups.

Mean differences between each pair of groups were compared for statistical significance, and the results are presented in Table 3.

Comparison of Groups I and II showed significant differences on both the verbal and the performance weighted score means, Group I having the higher value for the verbal weighted score and Group II for the performance weighted score. These differences were each significant beyond the 0.01 level of confidence. The total weighted scores for these groups were, however, nearly exactly the same. Differences between Groups I and II on the individual subtests were also generally significant. On the verbal subtests Group I had the higher means in each instance, and three of the six mean differences (Digit Span, Similarities, Vocabulary) were significant beyond the 0.01 level, with an additional mean difference (Comprehension) significant beyond the 0.02 level. With the performance subtests Group II did better than Group I in each instance. On Block Design the difference was significant beyond the 0.001 level, and on Picture Arrangement, Object Assembly, and Digit Symbol the difference was significant beyond the 0.05 level.

The results for Group III tended to correspond roughly with Group I on the performance subtests and for Group II on the verbal subtests. It is not surprising, therefore, to find that the only significant differences between Groups I and III occurred on the verbal subtests and the only significant differences between Groups II and III occurred on the performance subtests.

Discounting all cases in which verbal and performance totals were equal, in Group I, 26 of 33 patients (or 78.8%) had higher

TABLE 3.—*Mean Differences Between Wechsler-Bellevue Variables for Each Pair of Groups and Their Levels of Statistical Significance*

	Group I Minus Group II	Group II Minus Group III	Group I Minus Group III	Levels of Significance		
				I-II	II-III	I-III
Information	1.34	0.21	1.55	ns	ns	ns
Comprehension	2.46	0.48	2.94	0.02	ns	0.01
Digit Span	2.67	−0.83	1.84	0.01	ns	ns
Arithmetic	0.84	0.80	1.64	ns	ns	ns
Similarities	2.41	0.01	2.42	0.01	ns	0.05
Vocabulary	3.38	−1.52	1.86	0.001	ns	ns
Picture Arrangement	−1.87	1.36	−0.51	0.02	ns	ns
Picture Completion	−1.05	3.19	2.14	ns	0.05	ns
Block Design	−3.05	2.97	−0.08	0.001	0.01	ns
Object Assembly	−2.48	3.00	0.52	0.02	0.02	ns
Digit Symbol	−1.40	2.28	0.88	0.05	0.01	ns
VWS	9.72	0.61	10.33	0.01	ns	0.01
PWS	−9.28	12.45	3.17	0.01	0.01	ns
Total WS	0.38	13.14	13.52	ns	ns	0.05
Verbal IQ	11.44	−1.05	10.39	0.01	ns	0.02
Performance IQ	−10.18	12.13	1.95	0.01	0.05	ns
Full-scale IQ	0.85	6.30	7.15	ns	ns	ns

verbal than performance totals. On the contrary, in Group II, 13 of 17 patients (or 76.5%) had lower verbal than performance weighted score totals. A χ^2-test of the difference between these groups in this respect was significant well beyond the 0.001 level. Group III had 6 of 13 patients with higher verbal than performance totals. Comparison of Group I with Group III yielded a χ^2-value significant beyond the 0.05 level, but this occurred only because of the relatively large number in Group I with higher verbal than performance totals. Differences on this indicator between Groups II and III were not significant.

A further test of the significance between differences of verbal and performance weighted score totals was obtained through computing *t*-ratios. Difference scores between these variables were obtained for each subject. The mean differences in these distributions for Groups I and II were significant beyond the 0.001 level. The difference between Groups I and III just exceeded the 0.10 level, and the difference between Groups II and III was significant beyond the 0.01 level.

Intercorrelations of the sum of the verbal weighted scores, the sum of the performance weighted scores, and the total weighted scores were computed for each group and are shown in Table 4.

As would be expected from the lack of independence of variables, the verbal and performance weighted scores are in each instance highly correlated with the total weighted score. The correlations between verbal and performance weighted scores are approximately in line with expectation except in Group I, in which the coefficient just fails to reach the 0.05 level of confidence. As an additional step, the correlation between verbal and performance weighted scores was computed with Groups I and II combined. In spite of the frequent statement that an increase in heterogeneity of a group should cause an increase in the coefficient of correlation, a coefficient of 0.06 was obtained. The reason for this interesting result was visualized in a scatter diagram. The points in the scatter diagram for Group I, in which the verbal scores were considerably higher than the performance scores, effect a positive relationship by utilizing mainly the upper left quadrant of the scatter diagram. In Group II the performance scores were considerably higher than the verbal scores in general, and the lower right quadrant of the scatter diagram was principally used. While the points for each group individually defined a positive relationship of the variables, the effect of using principally the upper left and the lower right quadrants at one time was sufficient to reduce the coefficient to 0.06.

TABLE 4.—*Intercorrelations for Each Group of Verbal Weighted Score, Performance Weighted Score, and Total Weighted Score*

	VWS	PWS
Group I		
PWS	0.31	
Total WS	0.87	0.80
Group II		
PWS	0.67	
Total WS	0.93	0.89
Group III		
PWS	0.57	
Total WS	0.85	0.91

Comment

Group I, composed of patients who had difficulty in effecting the correct spatial configuration in attempting to copy a Greek cross, was clearly impaired on the performance subtests of the Wechsler-Bellevue Scale. Group II, composed of patients with dysphasia, was significantly better than Group I on the performance subtests but was impaired on the verbal subtests. For Group III, in which both dysphasia and difficulty with the cross were present in each patient, the results on the verbal and performance subtests corresponded approximately with the impaired level for each of the other groups.

Results from a number of other studies could be commented upon specifically with respect to the findings presented above. However, the relation of other results to the

present study must be considered with due care because of the use of different criteria for composing groups or because of different measuring instruments. Many of these studies have been concerned with regional localization of abilities in the brain. Critchley,[1] Brain,[2] Weisenburg and McBride,[3] Hécaen et al.,[4] and others have related disability in the composition or understanding of spatial configurations (similar to the difficulty shown by patients in Group I) to damage of the right cerebral hemisphere. Their criteria, however, for selecting and grouping patients were the regional locations of the brain lesion, whereas our criteria were the types of ability defect shown.

A recent study by Reitan[5] related cerebral lateralization of lesions to Wechsler-Bellevue results. In this study, Reitan found patterns of relationship on the Wechsler-Bellevue Scale in groups with clinically lateralized lesions that were strikingly similar to those of the present study. The combined information, then, suggests the possibility that lesions of the right hemisphere may impair such simple abilities as copying a cross, as well as the more complex tasks involved in the performance subtests of the Wechsler-Bellevue Scale. Lesions of the left hemisphere, on the other hand, may produce aphasia and/or impairment in the verbal subtests.

The differential relationship between levels of performance on the verbal and performance parts of the Wechsler-Bellevue Scale is of interest with respect to the apparent factorial composition of this test. Birren[6] and Cohen[7] have published independent factorial analyses based on groups differing in age and neurologic or psychiatric diagnosis. In each of these solutions the same subtests contributed to the first two factors extracted. They consisted exclusively of verbal subtests for one factor and of performance subtests only for the other factor.

The apparent consistency of these independent findings may lend increased emphasis to the results. It is important to note, however, that additional investigation is needed to establish in detail the validity of these various findings, whether or not specific factors, such as the type of lesion, may be of critical significance, and the appropriate limitations on generalization of the results.

Summary and Conclusions

Psychological testing of 221 patients with verified brain damage revealed that 64 (29%) showed clear disability in copying a simple Greek cross and 47 (21%) showed definite evidence of dysphasia. Twenty-one patients were defective in both of these respects. The frequency with which these losses in fundamental abilities occurred prompted an investigation of their more general significance.

The patients in each group had been given the Wechsler-Bellevue Scale of Adult Intelligence (Form I). The results indicated that the group composed of patients who had difficulty only in copying the spatial configuration of a Greek cross were clearly impaired on the performance subtests of the Wechsler-Bellevue Scale. One the other hand, the patients with dysphasia only were significantly better than the first group on the performance subtests but were impaired on the verbal subtests. The third group, in which both dysphasia and difficulty with the cross were present, gave results on the Wechsler-Bellevue Scale that approximated the impaired level for each of the other groups.

Other studies have been concerned with aphasia, difficulty in copying simple configurations, results on the Wechsler-Bellevue verbal and performance scales, and the differential effects of lateralized cerebral lesions. An integration of these various studies must be tentative because of the use of differing criteria for composing groups, as well as differing instruments for measurement. The hypothesis appears justified, however, that lesions of the right hemisphere, difficulty in effecting simple spatial configurations, and impairment on the performance subtests of the Wechsler-Bellevue

Scale are associated. On the contrary, lesions of the left hemisphere, dysphasia, and impairment on the verbal subtests of the Wechsler-Bellevue Scale tend to occur together. These hypotheses, of course, may be modified by many factors characterizing brain damage that have not yet been investigated under controlled conditions.

In consideration of the frequency of occurrence of "organic" language impairment and/or a difficulty in copying the spatial configuration of a Greek cross, it would appear that brief examinations for these types of impairment would be of value in routine application. The statistical analysis in this study indicates their differential relationships to results obtained on verbal and performance aspects of a measure of general intelligence (Wechsler-Bellevue Scale), and various previous publications suggest their possible value in lateralization of cerebral lesions.

Indiana University Medical Center, 1100 W. Michigan St. (7).

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Pallidotomy and Pallidoamygdalotomy in Certain Types of Convulsive Disorders

E. A. SPIEGEL, M.D.; H. T. WYCIS, M.D., and H. W. BAIRD III, M.D., Philadelphia

The importance of subcortical systems located as far down as the rhombencephalon for the propagation of corticofugal epileptic discharges became evident when it was demonstrated that the generalization of impulses originating in the motor cortex of one side was not prevented in dogs by median sagittal section of the prosencephalon, diencephalon, and mesencephalon (Spiegel and Falkiewicz [10]). Furthermore, it is known that not only the pyramidal tract (Hering,[20] in experiments on dogs) but also all the fiber systems contained in the cerebral peduncles are dispensable for the centrifugal conduction of cortically induced discharges (von Economo and Karplus [9] in cats). Thus, an extrapyramidal conduction of corticofugal impulses must play a significant part in the propagation of epileptic discharges; this was also suspected by Krisch,[28] on the basis of clinical observations. Important evidence in this direction has been presented by the recent experimental studies of Hayashi [19] in dogs and of Walker [16] in monkeys.

The ganglia of the extrapyramidal system may play a role not only in the propagation of epileptic discharges originating in the cortex but also as foci of origin of epileptogenic stimuli. This could be demonstrated by us [1,2] in a case of tuberous sclerosis associated with major and minor attacks. In this patient, x-ray studies revealed a single calcified focus localized by air studies in the area of the caudate nucleus, and stereotaxic lesions produced in the area of the calcification and in the adjacent pallidum practically eliminated the seizures. Experimental studies in monkeys (Facth, Walker, and Warner [10]) point also to the existence of such mechanisms.

Encouraged by these observations and by the finding of high-amplitude seizure discharges in the basal ganglia despite minimal changes in the scalp EEG (Spiegel, Wycis, Baird, and Szekely [42]), we studied the effect of stereotaxic pallidal lesions (pallidotomy) or combined lesions of pallidum and amygdala (pallidoamygdalotomy) in a selected group of epileptic patients.

The principles guiding us in the selection of these patients were (1) ineffectiveness of anticonvulsant medication and (2) the demonstration of seizure discharges in the basal ganglia, particularly the pallidum, or in this ganglion and in the amygdala. In order to demonstrate such seizure discharges, a slight sedation, as induced by tranquilizing drugs, was of value.

In studies on the human brain the number of depth electrodes that can be inserted is, of course, limited. We were particularly interested in the possible importance of forebrain ganglia and selected, therefore, the caudate nucleus, the pallidum, and the amygdala for electrographic studies. Occasionally thalamic electrodes were added.

Regarding the anatomical basis for these studies, it may be sufficient to mention that corticofugal fibers from the motor area and more anterior parts of the frontal lobe or their collaterals synapse in the striatum

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From the Departments of Experimental Neurology, Pediatrics, and Neurosurgery, Temple University School of Medicine and St. Christopher's Hospital for Children.

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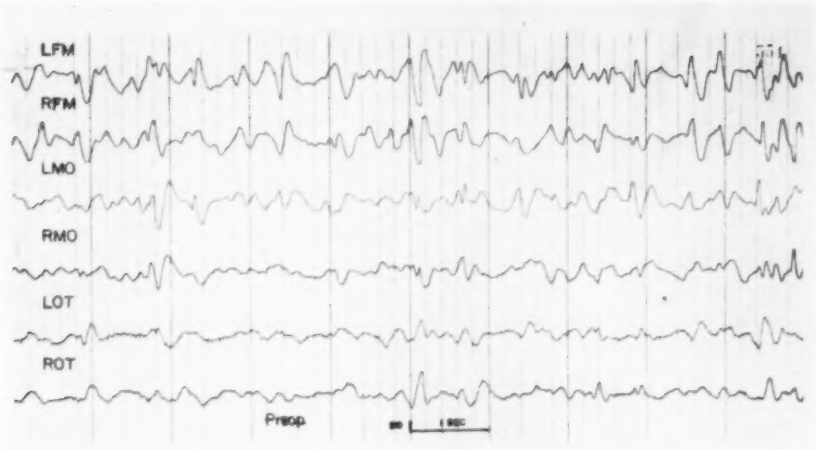


Fig. 1 (Case 1).—Preoperative scalp EEG.

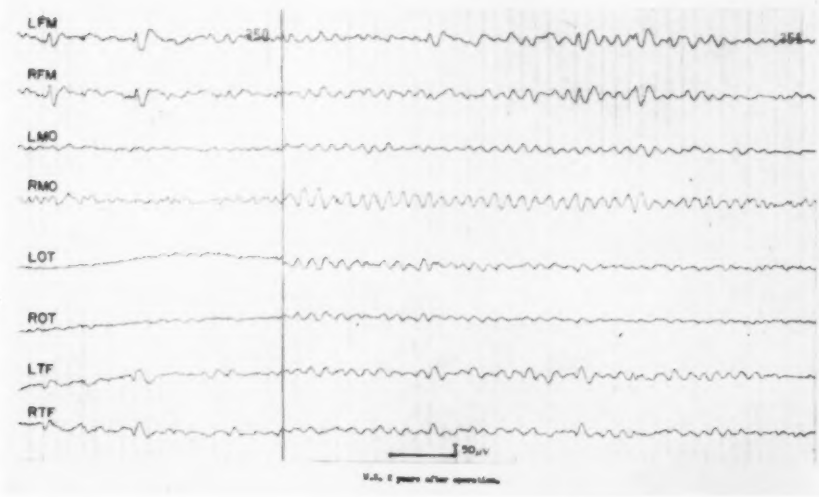
Abbreviations for this Figure, and for accompanying Figures, are as follows: *Am*, amygdala; *bp*, bipolar; *C*, caudate nucleus; *E*, ear; *F*, frontal lead; *l*, lower electrode (each depth electrode consists of an upper, a middle, and a lower electrode); *L*, left; *m*, middle electrode; *M*, motor lead; *O*, occipital lead; *P*, pallidum; *R*, right; *T*, temporal lead; *Th*, thalmus; *u*, upper electrode.

All standardizations in microvolts; time: 1 second.

(Ramón y Cajal [5]; Glees [16] Hirasawa and Kato [22]). The pallidum receives the majority of the efferent impulses from the striatum (Wilson [47]), and thus indirectly impulses from these cortical areas. Furthermore, it receives direct fibers from the frontal lobe (Levin [32]). Hayashi's [19] and Walker's [46] experiments are in agreement with these anatomical data. Strionigral fibers passing through the pallidum (Papez [37]) are also interrupted by a pallidal lesion.

Connections of the amygdala with the pyriform lobe (Johnston [26]; Crosby and Humphrey [8]; Lauer [29]), with the tip of the

Fig. 2 (Case 1).—Scalp EEG two years after pallidotomy.



temporal lobe (Klingler[27]), and with the insula (Ludwig and Klingler[33]) have been described anatomically. Electrographic studies suggest that these fiber systems conduct in corticopetal (Gloor[17]) as well as in corticofugal direction (Walker[46]). The participation of the amygdala in temporal lobe epilepsy has been noted in electrographic studies (Paillas et al[36]; Gastaut et al.,[14] and Brazier et al.[4]) and in stimulation experiments (Feindel et al.[11,12]). Accordingly, this ganglion has been included in operative procedures attempted in temporal lobe epilepsy (Chapman et al.[6]; Morris[35]; Penfield[38]).*

Method

For stereotaxic insertion of the recording and, later, of the lesion-producing electrodes, a small trephine opening over the frontal lobe proved sufficient. The method of inserting the electrodes has been described elsewhere.[42] No untoward effects were observed after these electrodes had remained in the caudate nucleus, pallidum, and amygdala for periods lasting up to one week. Depending chiefly on the results of depth electrography (mono- and bipolar records), stereotaxic electrolytic lesions were produced in the pallidum alone or in the pallidum and the amygdala. Preceding the production of the lesions, stimulation of the area to be eliminated was usually carried out in order to detect an undesirable position of the electrode (e. g., proximity to the internal capsule).

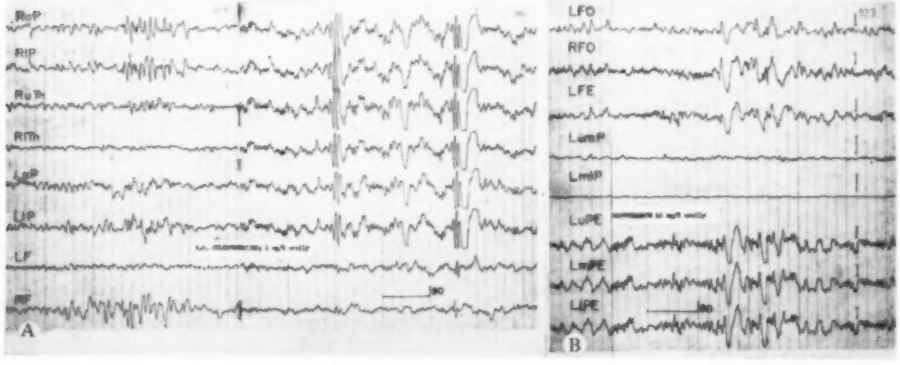
* Bailey et al.[3] uncovered the amygdala, as well as the hippocampus and uncus, in their temporal lobectomies but removed these areas only if spike discharges were recorded from them.

Results

Pallidotomy.—There were five cases in this series. Unilateral pallidotomy controlled the major and minor seizures in a child with tuberous sclerosis (Case 1); in a second child, with major and minor seizures of undetermined origin, only the latter were eliminated, while the major convulsions gradually returned (Case 2). The bilateral procedure was successful in an adult with cryptogenic seizures (Case 3). In two other cases, i. e., another child with tuberous sclerosis (Case 4) and an adult with convulsions due to scar formation following a cerebral abscess (Case 5), unilateral pallidotomy proved insufficient and production of additional subcortical lesions will probably be necessary. Table 1 summarizes the findings in this group.

Pallidoamygdalotomy.—In four cases lesions of the amygdala were added to those of the pallidum, since depth electroencephalography revealed seizure discharges in both groups of ganglia. In three cases (Cases 6-8), the pallidoamygdalotomy was performed only unilaterally, as a rule on the side where the seizure discharges were more pronounced. In the fourth case (Case 9) small bilateral lesions were produced in the anterior part of the pallidum; in a second

Fig. 3 (Case 2).—Scalp EEG, electropallidogram, and electrothalamogram. *A*, tracings under chlorpromazine sedation; *B*, under meprobamate sedation.



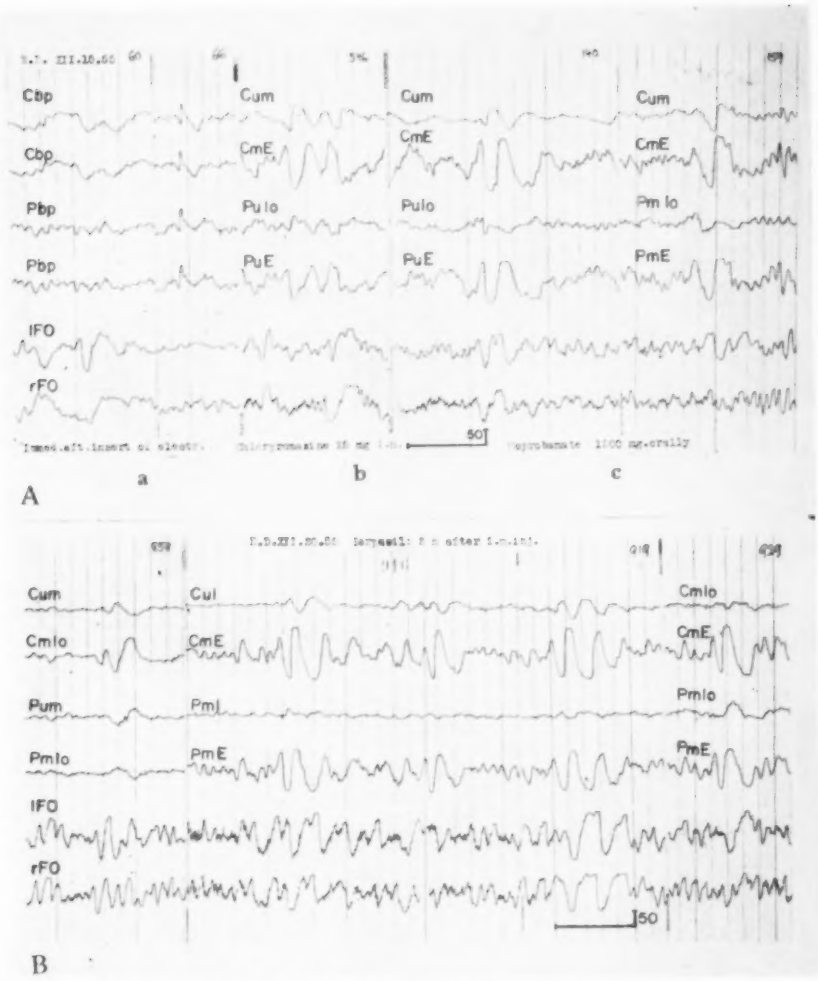


Fig. 4 (Case 5).—*A*, depth and scalp EEG (*a*) immediately after insertion of electrodes, (*b*) under chlorpromazine sedation, (*c*) under meprobamate sedation (*a*, *b*, and *c*, taken on different days). *B*, same patient under reserpine sedation.

stage, the right-sided pallidal lesion was increased, and lesions of the right amygdala were added. Whereas in the latter case the operative procedures proved insufficient, in the other three instances a definite influence of the unilateral pallidoamygdalotomy upon the appearance of the seizures was noted. In Case 6 the grand mal and salaam seizures did not reappear for the observation period of nine months, and only the fugue states were noted. In Case 7, there was a cessation of the myoclonic minor seizures for five months, thereafter, they reappeared at a reduced rate. In Case 8, there were, except for a grand mal seizure on the second day after operation, no more seizures for the duration of observation (four months). These cases are summarized in Table 2.

Comment

This report summarizes our preliminary experiences showing that in six of our nine

TABLE 1.—*Pallidotomies*

	Signs Symptoms	Scalp EEG	Depth EEG	Medication
Case 1, 10 yr., M	Tuberous sclerosis, mental retardation, adenoma sebaceum, tumors of fundus oculi; calcification in the right striatum	Repeated spike discharges in various leads against background of irregular delta waves (Fig. 1)	Seizure discharges, maximum amplitude, right pallidum	Heavy doses of phenobarbital, diphenylhydantoin (Dilantin), trimethadione (Tridione), Putnam's Dilantin. Narcosis failed to influence the seizures significantly
Preoperative	Generalized clonic-tonic convulsions (2-3 per wk.); about 250 minor seizures daily (nodding of head, extension of arms, flexion of waist)			
		Electrolytic Lesion in Right Caudate and Ansa Lentiformis		
Postoperative observation over 2 yr.	No seizures; better contact with environment; more easily manageable	More regular 4-6 sec. ryhthm; only occasional spikes, chiefly in the frontal leads (9 mo. and 2 yr. postop.) (Fig. 2)		Reduced to phenobarbital, 30 mg. b. i. d.; chlorpromazine, 25 mg. at bedtime
Case 2, 9 yr., M	Since 3 mo. of age, (1) almost daily tonic-clonic convulsions, (2) episodes of loss of postural tone (30-60 sec. duration), 3-6 t mes da ly	Multiple spikes in all leads; scalp discharges frequently less pronounced than pallidal & thalamic; no definite time intervals between spikes in subcortex & scalp	(1) Immediately after insertion under barbiturate anesthesia: very few abnormal pallidal discharges; (2) chlorpromazine sedation: high spikes in pallida r>l or all ganglia tested (Fig. 3); (3) meprobamate sedation: pallidal discharges slower	Phenobarbital, diphenylhydantoin, meprobamate, primidone, (Mysoline) acetazolamide (Diamox) did not alleviate the seizures
Preoperative	Subdural hygroma evacuated at age of 1 yr.			
		Right Pallidotomy		
Postoperative (observation period 1 yr.)	Grand mal seizures reappeared occasionally $\frac{1}{2}$ yr. postop., increased in frequency to 2-3 weekly; no minor seizures Patient more easily managed at home.	6 wk. postop.: practically normal; chiefly beta activity; 5 mo. postop.: some high sharp & slow waves, particularly in frontal leads 1 yr. postop.: multiple spikes in all leads		Reduced to phenobarbital, 30 mg. t. i. d., primidone, 25 mg. at bedtime
Case 3, 33 yr., M Preoperative	Since 15 yr. (1) general tonic-clonic seizures (2-3 weekly); (2) minor attacks with feeling of blood rushing to head (15 per mo.)	Mild dysrhythmia, some sharp waves; on hyperventilation 3/sec. waves in FM leads	High-voltage pallidal discharges	Heavy doses of diphenylhydantoin, phenobarbital; primidone did not prevent seizures
		Bilateral Pallidotomy		
Postoperative observation period 1 yr.-10 mo.	No major seizures; minor episodes reduced to 1 a month Transitory left-sided hemiparesis and transitory reduction in initiative Last dynamometric readings: R hand 11 kg.; L hand 9-10 kg. Patient a behavior problem	No significant changes		Reduced to phenobarbital, 30 mg. b. i. d.

Case 4, 6 yr., M Preoperative	Tuberous sclerosis, adenoma sebaceum (on bridge of nose and cheeks), phakoma in left optic disc Seizures (tonic extension of arms & neck, loss of consciousness) since 6 wk. of age, 10-15 /day	Spikes & slow waves, chiefly in frontal & temporal leads	Seizure discharges in right pallidum > in left	Phenobarbital up to 240 mg. per day; diphenylhydantoin up to 200 mg. a day; primidone, up to 500 mg. a day, did not completely control the seizures After trimethadione, phensuximide (Milontin), seizures severer
		Right-Sided Pallidotomy		
Postop. observation period 5 mo.	Seizures returned after 1 wk. Further lesions seem necessary	No significant changes		Phenobarbital, 30 mg. b. i. d.; diphenylhydantoin 50 mg.
Case 5, 24 yr., M Preoperative	Left post-traumatic frontotemporal abscess drained at age of 5; since age 16, (1) major seizures (head & eyes turn to the right, then gen. tonic-clonic convulsions), 3 per week; (2) minor seizures (unable to speak, followed by automatisms) about 40 a wk. Temporal lobectomy (Montreal Neurological Inst.) had only transitory effect	Focal discharges in the left frontocentral & temporal areas before temporal lobectomy; subsequently abnormal discharges in left inferior frontal region still present	Under sedation (reserpine, meprobamate, or chlorpromazine), seizure discharges in the basal ganglia (Fig. 4); great variability in relation of scalp & depth seizure discharges; former may precede or follow latter, or they may appear apparently independently of each other	Phenobarbital, diphenylhydantoin, and primidone do not control seizures
		Left-Sided Pallidotomy		
Postoperative observation nearly 1 yr.	Patient has still about 2 major seizures weekly & 4-5 minor seizures every other day; additional amygdaloid lesions are being considered	Sharp waves point to abnormal activity in remaining part of temporal lobe		Same medication

TABLE 2.—*Pallidoamygdalotomies*

	Signs and Symptoms	Scalp EEG	Depth EEG	Medication
Case 6, 6 yr., F				
Preoperative	Mental retardation; since age of 3 mo. seizures, (up to 500/day, av. 70/day): (*a*) flexion of arms, nodding; (*b*) falling; (*c*) staring spells; (*d*) fugue states with automatic movements Occasionally gen. tonic-clonic convulsions; ataxia on walking	High spikes & slow waves in all leads	Under reserpine: (*a*) high discharges in pallida & amygdalae with only slight alterations in scalp EEG (Fig. 5); (*b*) high scalp discharges preceding subcortical ones (Fig. 6), under promazine: (*c*) high discharges became pronounced in scalp later than in pallidum & amygdala (Fig. 7)	Phenobarbital, diphenylhydantoin, primidone, metharbital (Gemonil), meprobamate, alone or combined, ineffective
		Left Pallidoamygdalotomy		
Postoperative observation 9 mo.	No grand mal or salaam seizures; fugue states 1/wk. on awakening; mild right-sided hemiparesis; ataxia still present; behavior problem	10 days postop.: general slowing; no seizure discharges; 1 mo. postop.: groups of discharges of lower amplitude than before operation; 9 mo. postop.: spike component of seizure discharges less pronounced than before operation		Reduced to meprobamate, 400 mg. b. i. d.; mephobarbital (Mebaral) 30 mg. t. i. d.
Case 7, 4 yr., M				
Preoperative	Following vaccination, high fever, subsequently 50 seizures/day (flexion of arms, nodding); motor development arrested since 18 mo. of age	Almost continuous, irregular high spikes & sharp waves 1-4/sec. in all leads	Sometimes scalp (frontal) spikes preceded those in basal ganglia; sometimes scalp discharges followed those in pallidum & amygdala; high discharges, particularly in r. amygdala	Seizures uninfluenced by phenobarbital, 6 mg./kg.; diphenylhydantoin, 50-100 mg.; primidone, 125 mg. q. i. d.; paramethadione, 0.3 gm. q. i. d. trimethadione 0.3 gm. q. i. d.
		Right Pallidoamygdalotomy		
Postoperative observation ½ yr.	No seizures for 5 mo. without anticonvulsive medication; better contact with environment; 6 mo. postop. minor seizures at reduced rate (5-6/day); more distractable	½ yr. postop.: spikes & slow waves not continually as before operation, groups separated by flat record		

Case 8, 5 yr., F				
Preoperative	Following smallpox vaccination at 7 mo. seizures (nodding, extension of arms), 15-100 a day; last year 3-4 grand mal seizures; primidone stopped seizures for about 2 wk. only	High-amplitude spikes & waves 1-2 sec.	High seizure discharges in right amygdala & pallidum greater than in left, sometimes propagated to cortex, sometimes not (Fig. 8)	Daily: phenobarbital 180 mg., diphenylhydantoin, 200 mg.; primidone, 750 mg.; trimethadione, 1.8 gm.; phensuximide, 750 mg.; acetazolamide, 1 gm.; asparagine, 25 gm.; Mesantoin, 0.2 gm. in various combinations ineffective
		Right Pallidoamygdalectomy		
Postoperative observation 4 mo.	One grand mal following surgery; no further seizures	2 months postop.: frequency of spikes & high-amplitude waves reduced		Phenobarbital, 120 mg. a day; primidone 125 mg. a day
Case 9, 26 yr., M				
Preoperative	For 11 yr. seizures, 2-3 week, initiated by illusions, progressing to tonic spasms with opisthotonos	Moderate dysrhythmia	High-amplitude discharges in pallidum & amygdalae	Phenobarbital; diphenylhydantoin, primidone
		Lesions in Both Pallida and Right Amygdala		
Postoperative (observation ½ yr.)	Seizures were stopped for a few wk. only; additional lesions in left amygdala considered	No significant change		Same medication

cases (in three of the five pallidotomies and in three of the four pallidoamygdalotomies) seizures refractory to intensive drug treatment could be controlled or definitely reduced in frequency. It need not be emphasized that only long-range observations, extending for at least five years, will enable us to assess the possible therapeutic value of the procedures under study. Such a reservation applies particularly to the group of pallidoamygdalotomies in which the postoperative observation time ranged from four to nine months, while in the successful pallidotomies it extended over 2 years, 1 year, 10 months, and 1 year, respectively. In view of the possibility of applying our stereoencephalotome repeatedly exactly in the same position, we have in all cases, except Nos. 3 and 9 (with bilateral pallidotomy), produced the lesions so far unilaterally in the area of the most definite seizure discharges; it seems of interest that in five of the six successful cases the unilateral procedure was sufficient to influence the seizures favorably.

It should be noted that in some of the favorably responding patients the major convulsions (Cases 1, 3, 6) and in some the minor seizures (Cases 1, 2, 3, 6, 7, 8) were controlled by the operation, so that not only diencephalic systems (Jasper, in cats[25]; Spiegel and Wycis,[43] in patients with petit mal) but also forebrain ganglia may participate in the mechanism of some minor attacks.

In five of our patients the minor attacks showed either the fully developed syndrome of the so-called salaam convulsions (Clarke[7]), i. e., forward flexion of the head and trunk with elevation and abduction of the arms and/or flexion of the elbows, or rudimentary forms, such as falling to the ground, simulating a "loss of postural tone." In the literature one finds these types of seizures described under various names, such as atonic drop seizures or static seizures (Hunt[23]), akinetic or astatic seizures (Lennox[31]), and, more recently, propulsive petit mal epilepsy (Janz and Matthes[24]).

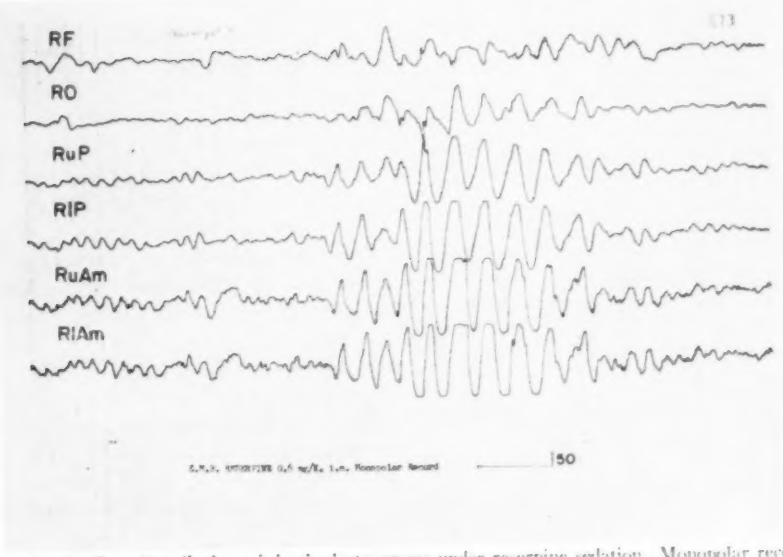
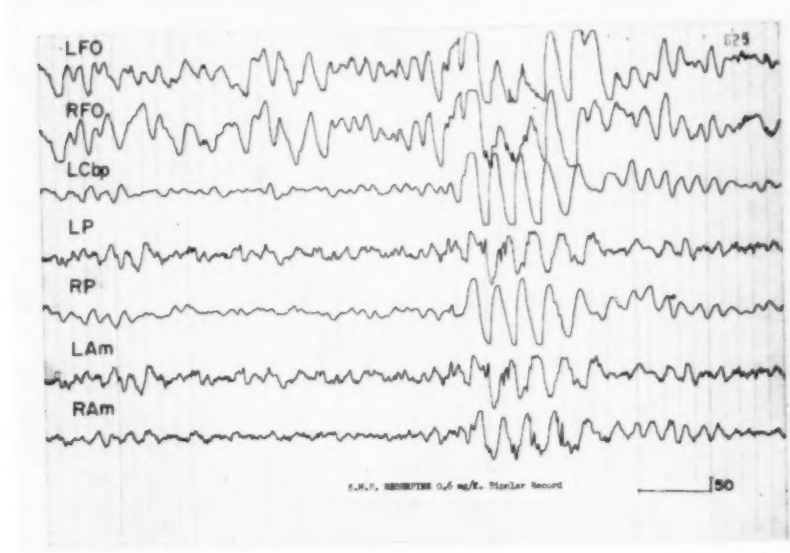


Fig. 5 (Case 6).—Scalp and depth electrograms under reserpine sedation. Monopolar record.

Penfield and Jasper[38] consider them as a form of myoclonic epilepsy. These various forms are apparently closely related and differ from each other only quantitatively, in the extent of the muscle groups affected and in the speed of the muscular contractions. Their pathogenesis is rather obscure, since autopsy reports have not contributed to an understanding of the underlying mechanism (hypoplasia of the cerebellum in one case, syphilitic meningitis, particularly over the central gyri in the second, moderate

Fig. 6 (Case 6).—Scalp and depth electrograms under reserpine sedation. Bipolar record.



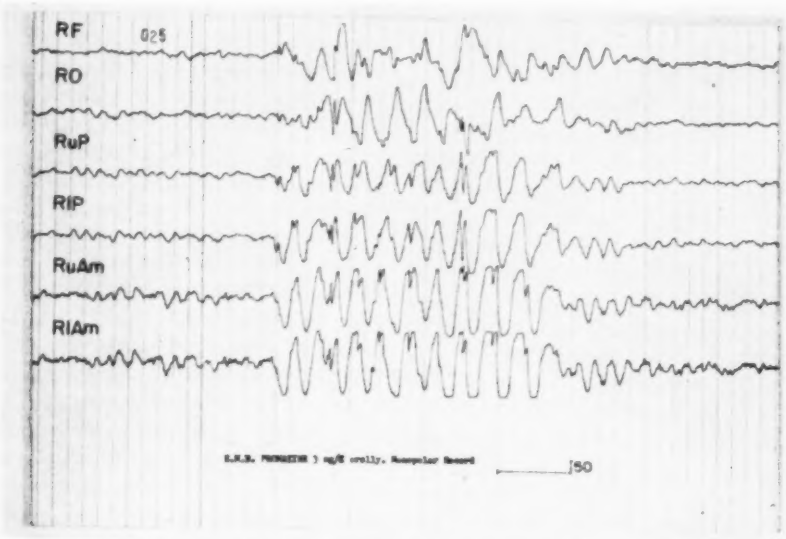
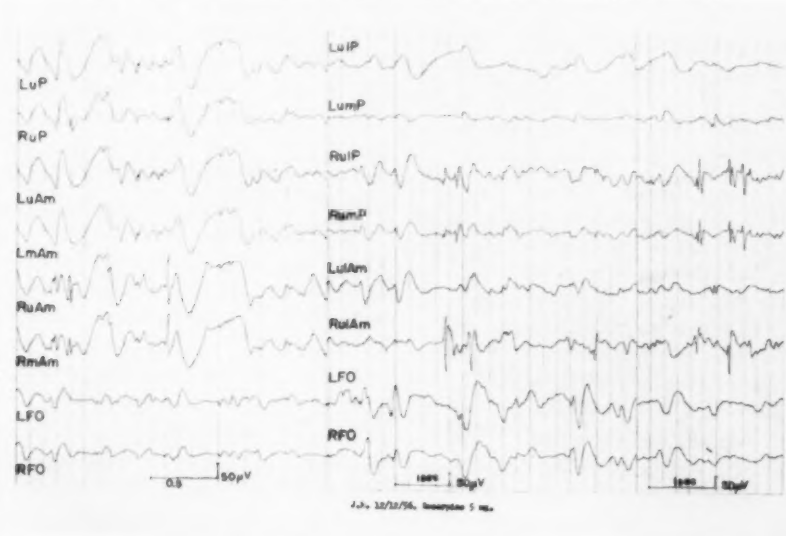


Fig. 7 (Case 6).—Scalp and depth electrograms under promazine sedation. Monopolar record.

hydrocephalus and pachymeningitis haemorrhagica in the third [24]). It has been pointed out by Lederer [30] that these seizures resemble the mass movements of the newborn and has been hypothesized that such mass impulses originate in the phylogenetically old pallidum. This hypothesis has been accepted by Zellweger,[48] whereas Janz and Matthes [24] believe that the entire extrapyramidal-cerebellar system is involved, and that these attacks are due to a "diaschisis of function serving the static innervation." These vague hypotheses show the uncertainty regarding the pathogenesis of these

Fig. 8 (Case 7).—Scalp and depth electrograms under reserpine sedation.



attacks, and it seems interesting, therefore, that in our material pallidal lesions eliminated this type of minor seizures.

Regarding the side-effects of the pallidotomies and pallidoamygdalotomies, there appeared neither tremor nor involuntary movements, nor definite changes in muscle tone. In one adult (Case 3), with bilateral pallidal lesions, a diminution of initiative was noticeable, which lasted, however, only a few months. In this case there appeared also a transient weakness of the left-sided extremities. In the mentally retarded girl (Case 6) there developed also a very mild hemiparesis. In children of this type it is, of course, hardly possible to perform the operation under local anesthesia and to observe the voluntary movements during the production of the stereotaxic lesions. Electric stimulation of the area to be eliminated preceding the production of the lesion is therefore of paramount importance, so that the position of the electrodes can be corrected if a stimulating effect upon the internal capsule appears. As a further safeguard, we now perform the lesions in such a way that the stylet of the electrode is never directed toward the internal capsule but is always parallel to this structure. Some of the children (Cases 1, 2) became more easily manageable and were in better contact with their environment (Cases 1, 7). This improvement probably is due partly to the diminution of medication and partly to the reduction of the secondary effects of the convulsions upon the cerebral activity.

The question may be raised whether it is justified to use the demonstration of seizure discharges picked up by depth electrodes as a guide for the production of lesions in the respective area. The study of scalp EEG's and of electrocorticograms is widely used by neurosurgeons in their efforts to locate removable epileptogenic areas, (Bailey and associates[3]; Penfield and Jasper[38]; Walker, Johnson, and Marshall[45]). Meyers,[34] though stating that spike discharges show a strong propensity to "wander" like a will-o'-the-wisp, admits the obvious need to explore extensively the clearly focal cases of epilepsy with deep, as well as surface, electrodes. If depth electrodes are used, one may object that their irritative effect may cause high-amplitude potentials: however, in numerous instances in which we inserted pallidal electrodes by the same technique in patients with nonconvulsive disorders, e. g., in extrapyramidal diseases, we have failed to observe high-amplitude seizure discharges similar to those obtained in epileptic patients. The question of the constancy of these findings in an individual case also needs some comments, particularly in view of Meyers'[34] above-mentioned statement. As a rule our patients were repeatedly tested receiving different types of sedation on different dates. Under these conditions, seizure discharges, for instance, in the pallidum, were a rather consistent finding (Figs. 3, 4), although the height and shape of the discharges differed for various types of sedation; for instance, higher and shorter discharges appeared with chlorpromazine than with meprobamate (Fig. 3). Another possible variation is that regarding the time relationship between the cortical and subcortical discharges (see below). The fact that an area such as the pallidum may act in one instance as a relay station of corticofugal impulses, as indicated by the sequence scalp discharges followed by pallidal discharges, and in another moment as an epileptogenic focus, as indicated by the reverse sequence, does not seem to militate against the inference that lesions should be produced in such an area but, rather, to support it. Therefore it seems justifiable to use the appearance of seizure discharges picked up by depth electrodes as a guide for production of stereotaxic lesions, particularly if this phenomenon is repeatedly demonstrable. The insertion of depth electrodes in several subcortical ganglia may be helpful by permitting one to identify an area with maximum amplitude of the seizure discharges and thus to define the localization of a focus with greater precision (Fig. 3 in our previous publication[2]).

Of course, the possibility of multiple foci has to be borne in mind. However, since it seemed desirable to keep the number of depth electrodes at a minimum, we placed them in ganglia where not only epileptogenic impulses may originate, but also impulses from other areas could be traced. The pallidum seemed the location of choice, because here fibers from the caudate nucleus, putamen, and frontal lobe converge; the amygdala was added, in view of its close connections with the temporal cortex. The hope that in these two sites a large part of the epileptogenic impulses may be detected and eventually eliminated has been, at least partially, realized.

The study of simultaneous electrograms from the scalp and from the depth of the brain seems of interest not only in that depth EEG's may show high-amplitude seizure discharges in the basal ganglia that are not at all, or hardly, revealed in the scalp EEG but also in regard to the time relationship between these seizure discharges. In cases in which the records show simultaneous scalp and depth discharges, the question must remain open whether one actually deals with simultaneous discharges in the various areas under study or whether a certain sequence of the discharges is masked by the relative slowness of the ink-writing system. Such records are not able to give us a clue regarding the origin and the propagation of the discharges. Of greater importance are observations in which the scalp discharges definitely precede those in the basal ganglia or, on the contrary, the scalp discharges follow those in these ganglia. The first type suggests a propagation of the impulses from the cortex to the subcortex, while the latter suggests an origin of the discharges in the subcortex, with secondary involvement of the cortex. Furthermore, the origin of the seizures may shift from the cortex to the subcortex, and vice versa, so that at one moment the subcortical discharges follow, while at another they may precede, those in the scalp, as could be observed in Cases 6 and 7.

The conclusion that a subcortically located epileptogenic focus may produce secondary discharges in the cortex is supported by the observation that following elimination of such a focus not only were the seizures diminished or abolished but also the scalp electroencephalograms showed a tendency to normalization. This applies particularly to the first patient with tuberous sclerosis, while in Cases 2 and 6 the favorable effect upon the seizures outlasted that upon the scalp EEG.

The anatomical basis for an influence of the basal ganglia upon the cerebral cortex is probably represented, at least partly, by fibers of the fasciculus lenticularis ascending in the fasciculus thalamicus and ending in the nucleus ventralis anterior and nucleus ventralis lateralis of the thalamus; from here the motor and premotor areas may be influenced. One also has to consider the importance of circuits passing through the hypothalamus and mammillary body, and thence by way of the dorsomedial and anterior nuclei, respectively, to the frontal and cingulate cortex. Electrical stimulation of the basal ganglia may alter the electrical activity of the cerebral cortex, as has been shown not only in animal experiments (Gerebtzoff [15]; Shimamoto [39]; Terzuolo [44]) but also in man. In patients in whom the ansa lenticularis and the ventral part of the pallidum were stimulated, Spiegel and Wycis [41] were able to elicit evoked potentials in the scalp EEG. Thus it becomes understandable that interruption of this circuit in the pallidum can at least diminish the influence of seizure discharges originating in the basal ganglia upon the cerebral cortex.

As mentioned in the introduction, this report is limited to a study of the participation of subcortical forebrain ganglia in the genesis and propagation of epileptic seizures and of the influence of lesions of the pallidum and amygdala on such seizures. It is, of course, possible that other ganglia may play a significant role in the generalization of epileptic discharges and act as foci of origin of epileptogenic stimuli. We have

to consider not only the diencephalon but also lower parts of the brain stem, as indicated by the experimental work (Spiegel and Falkiewicz [40]) mentioned in the introductory remarks. Further studies will have to approach these problems.

Summary

Pallidal lesions or combined lesions of pallidum and amygdala were produced in stages in nine epileptic patients selected because anticonvulsive medication was ineffective, and seizure discharges were demonstrable in the basal ganglia by means of depth electroencephalography.

The study of simultaneous electrograms from the scalp and from the basal ganglia showed variable time relationships; in some instances there were apparently simultaneous discharges in all these areas; in others, the scalp discharges preceded; in a third type, they followed the basal-ganglia discharges. This third type suggests the existence of subcortical foci producing secondary cortical discharges.

The postoperative observation period was four months to over two years. Unilateral pallidotomy was sufficient in two of four cases to control the seizures or to diminish their frequency. In one instance bilateral pallidotomy stopped generalized tonic-clonic seizures and drastically reduced the minor attacks. After unilateral pallidoamygdalotomy, in three cases the frequency of the seizures was significantly diminished; in a fourth, this procedure combined with a small lesion in the anterior part of the opposite pallidum was insufficient. For a proper evaluation of the possible therapeutic value of these procedures long-range observations will, of course, be necessary.

The favorable effect of pallidotomy was particularly striking in the so-called salaam convulsions of children. This observation seems to suggest that the basal ganglia play an important part in the mechanism of this poorly understood type of seizures.

The favorable effects of pallidotomy and pallidoamygdalotomy may be due to interruption of corticofugal impulses in the basal ganglia and/or to elimination of subcortical epileptogenic foci.

Temple University Medical Center, 3400 N. Broad St. (40).

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Books

Management of the Patient with Headache. By Perry S. MacNeal, M.D.; Bernard J. Alpers, M.D., and William R. O'Brien, M.D. Price, $3.50. Pp. 145. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1957.

This book is designed to present to the general practitioner information about the mechanisms of headache and its treatment. The authors emphasize the subjective aspect of the problem and stress the importance of the history of head pain as the way in which a specific diagnosis of the various types of headache can be made and through which the various headache mechanisms can be better understood.

The discussion of psychological mechanism is too analytical and pat for the average practitioner and may discourage his interest in this phase of the problem, but it does serve to point up this most important aspect of dealing with a patient with headache and the necessity for a complete personality investigation before any regimen of therapy can be successful.

The importance of headache as a symptom of "organic" brain disease is brought out, and details of the type, location, and severity of head pain in these disorders will be helpful in making a differential diagnosis.

Various types of "functional" headaches are discussed. The information presented for tension and vascular headache is clear and to the point. The arguments for "allergic headache" are not convincing.

Outlines for the treatment of the types of headache discussed are presented in detail. The authors take care to caution against extensive medical and surgical manipulations of the head and neck in the treatment of headache.

This book enters a field already crowded with excellent monographs on the subject of headache; but, despite the extensive competition, it is a helpful addition for the physician, who is daily faced with these problems.

FLETCHER MCDOWELL, M.D.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND NEW YORK NEUROLOGICAL SOCIETY

Morris Herman, M.D., Chairman, Section of Neurology and Psychiatry, Presiding

Combined Meeting, Jan. 14, 1958

Serum Reactions in Schizophrenia. Dr. Arnold Friedhoff, Dr. Myra R. Palmer, and Christine Simmons.

A study of the serum of 63 schizophrenic patients and 45 normal controls was undertaken in order to evaluate the effect of these sera on N,N-dimethyl-*p*-phenylenediamine. This procedure was originally introduced by Akerfeldt, who demonstrated increased oxidation of *p*-phenylenediamine (PPD) by schizophrenic serum. However, increased oxidation also occurs in other conditions, including liver disease, neoplasm, and pregnancy in the last trimester.

Results of our study indicate that schizophrenic serum oxidizes PPD at a significantly faster rate than the serum of normal controls. However, there is considerable overlapping of the two groups. Only 27% of the schizophrenic group had results that were higher than any of the normals. These results are in essential agreement with the data of Scheinberg and Horwitt, both of whom evaluated this procedure, using other methods.

As a result of these findings, we became interested in the effect of stress on the serum oxidase activity. We therefore studied the effects of electroshock treatment on the sera of 16 schizophrenic patients. The results of the Akerfeldt test, administered after a series of shock treatments, were significantly lower in 11 of the 16 patients than the results obtained before the series of treatments was begun. All sera used were fasting, and similar tests on a control group indicate that diet was not responsible for these results.

Discussion

Dr. Sidney Malitz: Although the Akerfeldt test is nonspecific, it may still have value in mental illness, provided our techniques are standardized and our diagnostic categories carefully described. In this study, no mention is made of the temperature of the reagent, proportion of serum to reagent, time when base line bloods were taken, or degree of severity and duration of the schizophrenic process. Our own findings with a group of predominantly acute schizophrenics showed an average optical density three times that of controls. Electroshock treatment in rats results in marked reduction of the ascorbic acid level in the adrenals. These data conflict with the hypothesis that the decreased optical density in Dr. Friedhoff's patients after EST is due to an *elevated* ascorbic acid level.

Dr. John R. Whittier: The oxidizing power of psychotic patients' blood and the overlapping by findings in nonpsychotic subjects have been reported before. Changes in oxidizing power during electroshock therapy and probable absence of influence by diet have not been reported before.

It is unreasonable to expect specificity of a biochemical test for a disease which itself lacks clinical definition. The value of this phenomenon lies in the possibility that positivity may be the reaction of *some* patients with psychotic diagnosis. Unless the "blood-brain barrier" is changed, the large size of enzyme molecules makes a primary role for the phenomenon unlikely.

Dr. Arnold Friedhoff: The bloods were drawn a few hours before the first shock treatment and the day after the last shock treatment. None of the patients had any tranquilizers or other medication except for the EST premedication. We have not completely ruled out the possibility that these drugs before treatment are responsible for the result.

As to whether the patients should be fasting or not, a diet with high ascorbic acid content, such as a glass of orange juice, does make a difference in the test.

As to the patients, we included both men and women, ranging in age from 29 to 67.

A Psychiatric Evaluation of Medical Student Selection. Dr. Richard N. Kohl and Dr. Charles A. Knehr.

A long-standing psychiatric service devoted to the counseling and treatment of students at Cornell University Medical College has given rise to a broad research program, which includes an evaluation of the various techniques of medical student selection. The appraisal of a student's nonintellectual characteristics constitutes the major problem of predicting his success as a student or as a physician. In an attempt to establish psychological testing as a valid selection device, investigators

at the Payne Whitney Psychiatric Clinic administered the group form of the Minnesota Multiphasic Personality Inventory to first-year students within one month after their admission to medical school. When the numerical scores of the separate scales of the MMPI were correlated with the final cumulative and average yearly standings of the classes as a whole, no significant relationships were observed. Although this test was found to be of limited value as a predictor of academic achievement and of the incidence of psychiatric illness, it did serve to indicate the presence of significant psychopathology. Such a test may be of considerable value if used in conjunction with the personal interview. The prediction of success in a medical career is dependent upon many factors, some of which are revealed through psychiatric treatment. Therefore, those psychiatrists responsible for treatment may well make a valuable contribution to the personal interview as a selection device.

Discussion

DR. OSKAR DIETHELM: In selecting a student for medical school, we are interested in choosing a healthy person, a person who promises to remain in reasonably good health and to become productive. The MMPI cannot tell us whether a subject is healthy or will remain healthy; it can merely give us indications with regard to his functioning at the time the test is taken. The diagnostic terms used in the test do not correspond to current psychiatric terminology. We cannot determine whether a schizophrenic illness will develop later or to what extent the student will mature during four years of medical school.

DR. ARTHUR ZITRIN: The absence of adequate criteria for success in a medical career makes it impossible to devise predictive tests for such success. Tests have been most helpful in prediction when we used the pass-fail criterion for success in medical school. The results of the MMPI are interesting, but I would caution against making them available to admissions committees. Interviewers may be misguided by test results wanting in precision. Long-term follow-up studies of medical graduates of the kind the authors and others are engaged in will eventually put our admissions procedures on a more rational foundation.

DR. RICHARD N. KOHL: I have no further comment, except to state that we hope that follow-up studies on the group of students now under investigation and the proposed study of psychiatrically ill physicians will help to clarify the criteria necessary for determining success in the practice of medicine.

The EKG and Respiratory Responses to Cerebral Angiography. DR. JOSEPH A. EPSTEIN, DR. BERNARD B. EPSTEIN, and DR. IRWIN HOFFMAN.

Eighty carotid arteriograms were performed on 35 patients suspected of having intracranial pathology. Serial electrocardiograms were made before, during and after the intracarotid injection of iodopyracet (Diodrast) and diatrizoate (Hypaque) to determine the cardiovascular effects of these compounds. The electrocardiographic responses obtained could be explained only on the basis of vagal stimulation and consisted chiefly of slowing of the sinus rate and of sinus pauses, followed by nodal escape and the development of nodal rhythm for as long as 30 seconds. The electrocardiographic responses obtained were severer using 35% and 40% concentrations of iodopyracet than with 50% solutions of diatrizoate. No response occurred with injections of saline.

Local infiltration of the area of the carotid sinus with procaine effectively eliminated the previously obtained vagal responses, suggesting that the afferent impulses responsible for stimulation of vagal centers in the medulla had their origin in the chemically sensitive carotid body.

These results indicate that the morbidity associated with this procedure may be related to the cardiovascular effects of these compounds. The area of the carotid bifurcation should be anesthetized before the performance of angiography in those patients in whom a fall in blood pressure or a change in cardiac rate or rhythm would be dangerous.

NEW YORK NEUROLOGICAL SOCIETY, AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Irving J. Sands, M.D., President, New York Neurological Society, Presiding
Combined Meeting, Feb. 11, 1958

Newer Techniques of Electrical Study in Neuromuscular Disease. DR. DANIEL S. FELDMAN, Philadelphia, and DR. I. H. WAGMAN.

When standard electrophysiologic apparatus, consisting of suitable amplifiers, recording systems, and biological stimulators, is used, the velocity of peripheral nerve conduction, the characteristics of the time course and the configuration of reflex activity, and the pattern of neuromuscular excitability can be studied in intact humans. These

techniques bring the observations of the physiologic laboratory closer to the patient and enable us to study physiologic processes when disease of the nervous system and the neuromuscular apparatus is present. They entail no risk and little or no discomfort to the patient and have provided significant information to our body of knowledge about the function of the nervous system. In addition, they appear to have diagnostic significance and offer objective methods for the evaluation of therapy.

Acutely Increased Intracranial Pressure: Experimental-Clinical Correlations. Dr. I. M. Tarlov, Dr. A. Giancotti, Dr. A. Rapisarda, and Dr. R. Coidan.

The development in our laboratory of new techniques to produce a gradually increasing mass and to record intracerebral pressure has led to this experimental study, the results of which were correlated with observations in patients suffering from acute intracranial hypertension.

These studies show that the Kocher-Cushing guides to severe acute intracranial hypertension—progressive slowing of pulse and respirations, increasing blood pressure, and gradually increasing unconsciousness—apply to certain expanding supratentorial masses; they do not accompany acute infratentorial tumefaction.

The most striking of these changes is the increasing fluctuation of blood pressure waves. Continuous recording of blood pressure (Lange arm-cuff method) may be helpful in distinguishing between acute supratentorial and infratentorial tumefaction and also in determining the course of patients suffering from the former type of lesion. Our experiments show, moreover, that the rise of blood pressure that may accompany acute intracranial hypertension in itself causes a further rise of intracranial pressure. This dangerous circular reaction can be broken, at least temporarily, by lowering the blood pressure. Precious time may thus be gained for palliative or definitive treatment.

Recording pressures alongside the midbrain in the tentorial hiatus, alongside the medulla, and within the cerebrum and cerebellum shows that the production of the Kocher-Cushing changes is related to a series of events, early among which is a transtentorial displacement of the midbrain. This point is important in relation to treatment. If a direct attack upon the lesion producing the displacement of the midbrain is impossible, then decompressing the midbrain by sectioning the tentorium and the incisura tentorii, or, preferably, by removing a part of the homolateral parietal or temporal lobe, or by making a large subtemporal decompression or sacrificing the bone flap may be life-saving.

Discussion

Dr. Sidney W. Gross: The experimental work of Dr. Tarlov and his associates is extremely important. Their results are borne out somewhat by clinical observation. We know, for example, that patients with extradural hemorrhage very often show the changes that Dr. Tarlov demonstrated in experimental animals, whereas patients with cerebellar tumors rarely do. Further observations by Dr. Tarlov and his group will very likely provide additional important data.

Dr. Fritz Cramer: I enjoyed this paper very much. The prospect of being guided by this planned bit of knowledge as to what is happening under certain conditions of changing intracranial pressure is heartening, in contrast to what we have to face clinically at one of the times when we are in the greatest quandary as to whether to operate or not—after an operation has been done and the patient has not regained consciousness, or has lost consciousness and a postoperative hematoma is suspected. Our judgment as to whether to operate cannot wait upon a complete syndrome of advancing pressure. I think that this work demonstrates well that a relentless change in any function, whether it is in blood pressure, in respiration, or in pulse, or whether it is loss of consciousness, warns that there is a change within the centers that control these factors, and that is the indication for going ahead.

Dr. William M. Manger: What was the midbrain pressure in the balloon before the Kocher-Cushing phenomena were noted?

Dr. Howard Freedman, Brooklyn: I enjoyed Dr. Tarlov's presentation very much. I should like to point out the importance of the consideration of the midbrain in problems of supratentorial pressure. One of the slides indicated alterations in respiration associated with lowering of the lumbar thecal pressure, demonstrating the importance of the relative pressures in the supratentorial and infratentorial spaces in changing something in relation to the midbrain or brain stem, whether it be the circulation of the brain stem or actual pressure on the brain stem itself. I point out again the clinical importance of caution in lowering spinal fluid pressures in cases of supratentorial mass lesions.

Dr. Morton Nathanson: I should like to comment on the other aspect of this interesting study. Under the same conditions, 40% of the animals showed no uncal herniation and 70% showed no medullary compression. I think it is of importance to study that group as well, since the entire problem of intracranial pressure, papilledema, fluctuating states of consciousness, and spinal fluid pressure certainly is not clear. We might also ask why 23 of the 40 patients who had increased intra-

cranial pressure and neoplasms did not show these phenomena.

With regard to the pressure of the midbrain, is not the balloon actually outside the midbrain, and is Dr. Tarlov not measuring the pressure in the subarachnoid space?

DR. I. M. TARLOV: The pressure outside the midbrain—subdural, and not subarachnoid—was about 100 mm. of mercury before the Kocher-Cushing changes occurred. We have the work on 60 animals, 40 with supratentorial and 20 with infratentorial compression, and never with infratentorial compression did we see the Kocher-Cushing changes.

While only 60% of the dogs with supratentorial compression showed uncal herniation, they all showed histologic abnormality of the midbrain. In 12 cases out of 15, the damage to the midbrain was greater than to the medulla, and in the remaining 3 dogs it was about the same. On the other hand, the dogs with subtentorial compression showed more damage to the medulla.

DR. MORTON NATHANSON: Did any of the animals show papilledema?

DR. I. M. TARLOV: We have not yet undertaken funduscopic examinations in our animals.

Electroencephalography in Carotid Thrombosis and Cerebrovascular Insufficiency. DR. E. S. GOLDENSOHN, DR. WILLIAM K. HASS, and DR. ELLIOT WEITZMAN.

The 35 cases of carotid occlusive disease reported were a consecutive series of patients at the Neurological Institute of New York having at least one EEG and verification of the diagnosis by angiography (32 patients), surgery (1 patient) and autopsy (2 patients). The left internal carotid artery was the site of the lesion in 20 cases; the right, in 11. The vessels were completely occluded in 27 and markedly narrowed in 4. In addition, two had bilateral internal carotid and two had common carotid involvement. The EEG's were performed hours to years after the most recent exacerbation of symptoms. Six patients had normal and twenty-nine had abnormal records.

The EEG abnormalities were mainly of the focal marked slow-wave variety, such as is often found in brain tumor. Some cases showed voltage depression only. The degree of EEG abnormality generally paralleled the severity of neurological deficit. The frequency occurrence of abnormalities in carotid occlusion was 83%, and not significantly different from that of brain tumor. Persistent severe abnormalities often lasted for months to years.

In addition, the effects of postural tilting on 23 patients, including 7 with proved carotid artery occlusion, were examined. Up to now we have found that postural tilting has added no information beyond that of the resting record in the diagnosis of internal carotid occlusion. The value of the resting EEG in vascular disease may be to localize the lesion and to divide carotid and main-trunk middle cerebral occlusion and tumors, on the one hand, from smaller-branch vascular accidents and early impending infarctions, on the other.

Discussion

DR. HARRY ARTHUR KAPLAN, Brooklyn: We are interested in somewhat the same problem that Dr. Goldensohn and his colleagues are working with. Our thoughts are somewhat along the same lines concerning swelling of the brain associated with intracranial masses. Certainly, when occlusion of the carotid artery occurs, it is not only the cortex that is implicated, but the whole of the area, including the white matter. Thalamocortical tract disturbance probably accounted for the depression seen on the EEG in the case with bilateral slowing and lower voltage on the side of the lesion.

DR. MILTON N. TARLAU: In the last year we have seen at least three cases of thrombosis of the internal carotid in its cervical portion, all with clinical signs, but all three showing only very mild EEG changes, consisting chiefly of slowing of the alpha activity on the affected side. In all, arteriography demonstrated collateral circulation through the ophthalmic artery with filling of the middle cerebral artery. There may also have been collateral circulation from the opposite side. It seems to me that this collateral circulation accounts for the minimal EEG findings. Did Dr. Goldensohn have the opportunity to correlate his findings with the presence or absence of collateral circulation?

DR. E. S. GOLDENSOHN: In answer to Dr. Kaplan, the brain of one of the patients whose EEG showed voltage depression was subjected to pathologic examination. In addition to multiple areas of old encephalomalacia in the frontal and parietal lobes, fresh softening was observed in the temporal and occipital lobes and, more deeply, in the insula, external capsule, claustrum, and lateral putamen. We do not know whether this subcortical involvement contributed to the voltage depression or whether subcortical involvement was present in the other cases which showed voltage depression.

In answer to Dr. Tarlau's question, we have not found a significant relationship between collateral circulation by way of the ophthalmic artery and the EEG. The group with evidence of ophthalmic collateral circulation showed about the same incidence of slow-wave abnormalities as did the rest of the series. There was no apparent relationship between the degree of collateral supply and the extent of functional loss.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY; NEW YORK NEUROLOGICAL SOCIETY, AND NEW YORK SOCIETY FOR CLINICAL PSYCHIATRY

Morris Herman, M.D., Chairman, Section of Neurology and Psychiatry, Presiding

Combined Meeting, March 11, 1958

Electrolyte Changes Induced by Thyroid Administration in Psychiatric Patients. Dr. Frederic F. Flach and Dr. Oskar Diethelm.

The administration of triiodothyronine to selected psychiatric patients seems to be often associated with the appearance of hostile emotions and sexual strivings, increased psychological activity, and aggressiveness. Concomitantly, psychopathologic features of diminished emotional responsiveness, denial of the experiencing of emotions, depersonalization, withdrawal, and obsessive-compulsive symptoms may be significantly reduced. Depression of mood may be alleviated, except where it constitutes the central psychopathologic condition, as in depressive mood disorders.

In order to clarify mechanisms whereby triiodothyronine may evoke or intensify the above-mentioned emotions, selected patients were placed on the metabolic unit of the Payne Whitney Psychiatric Clinic. There they were maintained on constant controlled diets, while all urines and stools were analyzed for nitrogen and electrolyte content.

Three of these patients have been presented. Periods of intense emotion (particularly hostility and, to a less extent, anxiety), related to triiodothyronine administration, seemed to be associated with a shift to negative calcium balance, largely due to calcium loss in the stool. When emotions subsided, a shift to calcium retention was noted. These alterations in calcium metabolism may be fundamental mechanisms or may only reflect other related biochemical activity.

It remains to be clarified whether calcium loss is also associated with strong emotions in other experimental settings, and whether a different metabolic effect may be seen when triiodothyronine does not induce these strong emotional and psychopathologic changes.

Discussion

Dr. Oskar Diethelm: I might give a brief idea of how we got started on this project. Apathy and depersonalization in schizophrenic patients have long been considered as possibly related to hypothyroidism. We felt these symptoms should be related not to a nosological entity but, rather, to psychopathologic states. We therefore study depersonalization when it occurs in schizophrenic, depressive, and psychoneurotic conditions. The erotic behavior which we noticed in the presence of this drug interested us greatly because erotic behavior is unusual in depression, although it definitely may occur.

Experimental Studies of Convulsive and Drug Therapies in Psychiatry: Theoretical Implications. Dr. Max Fink; Dr. Robert L. Kahn, and Dr. Martin A. Green.

In studies of convulsive, psychopharmacologic, and insulin coma therapies, evidence for a neurophysiologic-adaptive hypothesis of the mode of action of these therapies, has accumulated. This hypothesis ascribes the efficacy of each therapy in the treatment of psychoses to their ability to induce a persistent alteration in cerebral function, which provides the milieu for a change in adaptation of the subject to his environment. In these studies, analyses of changes in the electroencephalogram have been used as indices of altered brain function.

In convulsive therapy, the shift in EEG frequencies to the delta range has been directly related to the behavioral change. A similar relationship has been observed in insulin coma. Various psychopharmacologic agents can be classified according to the EEG effects induced: (*a*) a shift to delta frequencies (chlorpromazine, promazine, perphenazine, and high-dose reserpine); (*b*) a shift to fast frequencies, with increased synchronization (meprobamate, barbiturates), and (*c*) desynchronization of frequencies (diethazine, benactyzine, and mepazine).

From these analyses, a shift in EEG frequencies to delta range and increased synchronization are suggested as the neurophysiologic concomitants of tranquilization and sedation. The neurophysiologic-adaptive hypothesis has application to the management of physiodynamic therapies, screening of psychopharmacologic agents and as a frame of reference for the study of behavior and neurophysiology.

Discussion

Dr. William A. Horwitz: Any attempt to correlate clinical changes solely with altered brain functioning oversimplifies this problem. Many patients receiving electroshock therapy do have altered brain function, as evidenced by the clinical picture and electroencephalographic findings. This is also true in other treatments, such as insulin coma therapy, and more so in protracted coma, where there is frequent clinical improvement in the presence of an even greater degree of altered brain function.

On the other hand, in some clinical syndromes, intensive treatment may result in an even severer disorganization of brain function, with no improvement, or only temporary clinical improvement evidenced.

Therefore, the thesis that alteration in brain functioning is the primary factor responsible for improvement appears to have limitations. It does not explain why patients with certain syndromes, such as depressive states with alteration in brain functioning, do recover, whereas schizophrenics or patients with severe obsessive-compulsive psychoses, who may show an equal or greater alteration of brain function, do not maintain their improvement.

DR. JOSEPH D. SULLIVAN: Chlorpromazine and similar drugs and the Rauwolfia derivatives are in the first group which lead toward increase of delta activity; the barbiturates and meprobomate lead to a beta shift, and mepazine and benactyzine are in the third group, producing desynchronization.

DR. MARVIN S. BELSKY: What is the effect of the tranquilizers on the EEG's of normal people? Is there any relation between the pretreatment EEG and the effect of the drugs and the dosages given?

DR. MAX FINK: The common basis for the mode of action of various forms of somatic therapies is that they induce an alteration in brain function; they do not induce improvement. Altered brain function provides the stage in which the changes in behavior occur. Personality differences among the subjects referred for treatment provide the differences in behavioral response which we evaluate as to "improvement."

In these studies, changes in the EEG are only one index. Memory scales, perceptual tests, both visual and tactile, and language tests are indices of altered brain function, and for each there is a correlation between changes in the tests and the *behavioral* response. In each, however, personality aspects are the second factor in the *improvement* response.

In reply to Dr. Sullivan, the EEG pattern of various drugs was recently summarized in the *Journal of the Hillside Hospital*, October, 1957.

Dr. Belsky's question highlights the problem of the relation between the pretreatment EEG and both the EEG and the behavioral response. We have recently found a significant correlation between the pretreatment per cent time alpha activity and the degree of delta activity induced in the fourth week of treatment.

A Study of Interactions Between the Child's Intrinsic Reaction and Environmental Forces. DR. ALEXANDER THOMAS and DR. STELLA CHESS.

An ongoing longitudinal behavioral study of 82 children is reported, with data suggesting that each child has a specific type of reaction pattern to environmental stimuli, which shows itself in the first few months of life and which persists in a stable, consistent form throughout infancy and later childhood. Because of differences in life situations and levels of maturation as the child grows older, the same reaction pattern will show itself in very varied forms in actual behavior at different age periods. The data for the behavioral analysis are obtained by detailed histories taken in a specific objective and factual fashion from the parents at frequent intervals plus periods of direct observation of the child's behavior. The classification involves (1) quality of responses, whether predominantly positive or negative, and whether predominantly quiet, moderate, or intense; (2) manner in which consistent, long-term responses are developed; (3) modifiability of responses; (4) general activity level, and (5) threshold of sensory responses.

The specific history-taking technique which has been developed appears capable of yielding both detailed and accurate data. A qualitative analysis of the data, and a quantitative item analysis in 22 cases indicate a high order of correlation of the reaction patterns at different age periods. The available evidence, though as yet very scanty, suggests that these patterns are inborn and not experientially determined. A number of brief examples from the material are given to indicate that the child's own reaction pattern may significantly influence both the nature of the impact of environmental stimuli on him and the behavior and attitudes of his parents and other significant people in his environment.

Discussion

DR. AARON H. ESMAN: Such studies as this promise to contribute to the settlement of the question of the roles of nature and nurture in the individual's development, and may cast light on the baffling problem of choice of neurosis. I have some question about the use of history-taking as the primary source of data in such a study, due to the possibility of distortion by the parents of some of the data through selective inattention or selective focusing. Ideally, direct observation beginning at or before birth should be extended to all cases to rule this out. Once a particular response pattern has been elicited in a particular child, it might be fruitful to attempt to predict the child's reaction to certain crucial life situations and see what happens.

Impressions of Soviet Psychiatry*

ZIGMOND M. LEBENSOHN, M.D., Washington, D. C.

With the recent increase in cultural and scientific exchange between the United States and the U. S. S. R., there has occurred a corresponding increase in the interest of American psychiatrists in obtaining a better understanding of what is now going on in Soviet psychiatry. The following report was written not only to give American readers a brief glimpse into the current directions of psychiatric activity in Russia but also to indicate some of the practical difficulties and stimulating rewards encountered in making a trip for such a purpose.

This paper, then, is a report of my impressions of Soviet psychiatry gained during a 10-day visit to Moscow and Leningrad from Sept. 13 to 23, 1957. The trip was made as a medical tourist traveling privately, paying the standard Intourist rate of $30.00 per day. Since this included de luxe accommodations, meals, and the services of a car, driver, and interpreter, the rate did not seem exorbitant. During the Moscow portion of the visit, I inspected psychiatric facilities in the company of Prof. W. Horsley Gantt, M.D., Director of the Pavlovian Laboratory at The Johns Hopkins University School of Medicine, and Eugene Ziskind, M.D., Professor of Clinical Psychiatry at the University of California School of Medicine at Los Angeles. Professor Gantt, by virtue of his having worked with Professor Pavlov (1925-1929), his well-known work on conditioned reflexes, and his knowledge of the Russian language, provided us with an invaluable entree to the leading research centers of the Soviet Union. A letter which I had received from the Ministry of Health, U. S. S. R., assuring me of their willingness to assist me in visiting the various psychiatric centers in which I was interested, and numerous letters of introduction to Soviet medical leaders proved to be totally useless. Had it not been for Professor Gantt's presence, it is doubtful whether any significant appointments would have been arranged.

Despite Dr. Gantt's knowledge of the Russian language, all appointments were made by and through our Intourist interpreter-guides, who also accompanied us to all our meetings. With rare exception, they remained with us during the interviews and inspection tours, even though all the Russian scientists interviewed spoke English, German, or French, with facility ranging from fair to excellent.

In Moscow the following four professors were interviewed by the three of us: (*a*) Prof. P. K. Anokhin, Professor of Physiology at the University of Moscow School of Medicine; (*b*) Prof. E. A. Popov, Professor of Psychiatry and Director of the

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Professor of Clinical Psychiatry, Georgetown University School of Medicine.

Although these disclaimers may be completely gratuitous, I should like to say that the opinions expressed in this report are entirely personal and do not reflect the position of any organizations or institutions with which I am associated.

* Special article.

Psychiatric Clinic of the First Moscow Medical Institute, named after Korsakov; (*c*) Prof. A. R. Luria, professor of psychology, Moscow University and Director of the Institute of Defectology, and (*d*) Prof. S. A. Sarkisov, Director of the Institute of the Brain, Moscow, and member of the Academy of Medical Sciences.

On Sept. 18, Drs. Gantt and Ziskind left Moscow for Kiev. I remained an extra day in Moscow for the express purpose of (*a*) visiting one more psychiatric hospital and (*b*) visiting the Serbskii Insitute of Forensic Psychiatry. Our cordial experiences with the aforementioned professors had led me to believe that it would now be relatively easy to arrange for such visits. This proved to be an example of completely naïve reasoning in the Soviet Union. In spite of two personal telephone calls to Professor Popov, plus numerous attempts on the part of my interpreter to contact the Ministry of Health, the director of the Serbskii Institute, or the director of any of the various psychiatric hospitals, it remained, in the end, completely impossible to arrange for either of these visits.

In Leningrad I was able to confer with two well-known leaders of psychiatric and psychophysiological research, as well as with several of their distinguished assistants. The two chief scientists were (*a*) Prof. K. M. Bykov, Director of the Institute of Physiology, named after Pavlov, and member of the Academy of Sciences of the U. S. S. R., and (*b*) Prof. P. S. Kupalov, Department of Physiology of the Institute of Experimental Medicine. Through the courtesy of Professor Bykov, I was taken through Pavlov's old laboratory at Koltushi by Dr. M. N. Pototsky, a research biologist on his staff.

Once an appointment was made, we were invariably received with cordiality and treated with courtesy and respect. In general, the language problems did not prevent genuine exchange of ideas with the aforementioned scientists, since all, with rare exceptions, spoke quite good English.

The interviews will be reported in chronological sequence, followed by a general discussion. At times, especially when the person interviewed spoke very slowly, it was possible to record verbatim remarks. Whenever this occurred, the statements will be placed in quotation marks. Occasionally I have inserted a word or supplied a phrase to make the meaning more clear. Such inserts will be set off by parentheses.

Our first interview, on Sept. 16, was with Prof. P. K. Anokhin, Professor of Physiology at the University of Moscow. Professor Anokhin had known Dr. Gantt in the late 20's, when both were working with Professor Pavlov. We were warmly welcomed by Professor Anokhin in his book-lined office at the University. Professor Anokhin is a large, friendly, outgoing man with a ruddy complexion, in his late 50's. He was very active and energetic in his manner. On the walls of his office were several portraits and two busts of Pavlov, and also a portrait of Sechenov, the father of Russian physiology. (There were also paintings and busts of Lenin, Stalin, and occasionally Marx and Engels, in this and in almost every institution we visited.) The "cult of personality" (in physiology and medicine, at least) seemed to be flourishing wherever we visited. Professor Anokhin took us through the laboratories which were housed in the old section of Moscow University, which is within sight of the Kremlin. The apparatus seemed adequate, but on the whole there seemed to be less emphasis on equipment than on theory and method. We were escorted through the physiological museum, which housed much of Sechenov's old laboratory equipment and manuscripts.

We then returned to Professor Anokhin's office for tea and cakes, posed for photographs, and proceeded to the discussion of research. He discussed recent experiments on the effect of chlorpromazine (which is called Aminasin in Russia) on experimental neuroses in rabbits. Normal rabbits, showing normal EEG patterns, were given slight

electroshocks, sufficiently strong to produce desynchronization of the EEG pattern, but not strong enough to produce convulsions. After this procedure, the rabbit refused to eat and would not even touch carrots. The rabbit was then given an injection of chlorpromazine, and after this he began to eat avidly. Experimental evidence indicated, according to Professor Anokhin, that the site of action of chlorpromazine was in the reticular formation.[1]

Professor Anokhin proposed the theory that neuroses are produced when opposing stimuli and opposing reflexes are produced which increase to greater and greater power but still remain of almost equal strength. Chlorpromazine acts by blocking one set of reflexes, permitting the unopposed action of the remaining set. He drew diagrams in the classic Pavlovian tradition to explain his thesis. Professor Anokhin emphasized several times that his diagrams, theories, and plans were "not speculative" but were based on definite objective experimental data.

Further discussion centered about a paper entitled "The Coming Choice for Psychiatry," by Gwinn Owens, which appeared in a recent issue of the *Johns Hopkins Alumni Magazine*.[2] Curiously enough, Professor Anokhin had the magazine itself and was familiar with the content of the article, which dealt with the conflict between the Freudian and the Pavlovian approach. He seemed chiefly interested in knowing which approach represented the present trend in American psychiatry. He spoke highly of Dr. Chauncey Leake, who visited Russia in 1956 and published a brief report on his findings in *Science*.[3] Professor Anokhin then promised to set up appointments for us with Professors Popov and Luria for the following day and also made arrangements to see Drs. Gantt and Ziskind once again on their return from Kiev.

The following morning, we were taken to visit Prof. E. A. Popov, one of the most active and best-known clinical psychiatrists in the Moscow area. He is the director of a small, 150-bed teaching hospital, where a great deal of training and research goes on at all times.

Professor Popov was a stocky, heavy-set man in his 50's, with closely cropped hair and heavy-rimmed glasses. He received us cordially in his office, wearing the customary white smock of the European hospital doctor. Our visit was composed of three parts: (1) a discussion of general trends and principles governing psychiatric treatment and research in the Soviet Union; (2) a tour of the hospital (on which we were provided with white smocks and were guided by Professor Popov himself); and (3) a "question-and-answer" period after our return to the office.

I. General Trends

Professor Popov spoke in slow, halting, but deliberate English. At times it was possible to take down his comments verbatim in longhand. From time to time he sipped from a glass of cool tea as if to moisten his lips. He introduced us to one of his colleagues, Prof. V. M. Banshikov, President of the Moscow Society of Neuropsychiatry, who stayed with us briefly.

Professor Popov immediately established that he was well acquainted with the research work of Dr. Gantt on conditioned reflexes, as well as the work of Dr. Ziskind on insulin. He said his clinic (hospital, in the American sense) was founded in 1887. It was designed by Kojevnikov, and its first director was Korsakov, whose name is now attached to the institution. Portraits of Pavlov and Korsakov adorned the walls of his small and modest office.

"Now the trend in Soviet psychiatry is the application of the principles of higher nervous system activity based on Pavlov's teachings. This is one of the clinics of the First Medical Institute. We teach students on three levels: (*a*) basic psychiatric research; (*b*) treatment of patients, both inpatients and outpatients, and (*c*) postgraduate teaching."

He continued:

"The main problem is schizophrenia. We approach the problem from five main angles: (1) electrophysiological; (2) conditioned reflexes;

(3) investigation of the speech of schizophrenics; (4) neuropathological, and (5) biochemical.

"All investigations are united on the basis of *one* hypothesis. We have three branches of the work going on at this Institute. (*a*) Clinical and physiological: Inhibition of the higher levels of the central nervous system is a general trend which we find in the clinical picture of schizophrenia. We have as a base the Pavlovian conceptions on the nature of schizophrenia. For example, in catatonic states we have a picture produced by inhibition of the cortex and disinhibition of subcortical levels. Schizophrenic thinking is like 'dream thinking.' This is an old thesis of Eugen Bleuler, Schneider, and others. *But* for these others it was a plain empirical fact. For us it has a different meaning; namely, *thinking* in the dream state is a result of the particular inhibition of the cortex, and schizophrenic thinking is also a result of particular inhibition of the cortex. The two depend on similar causes. (*b*) Vegetative nervous system: In schizophrenia we have a predominance of the parasympathetic over the sympathetic nervous system, as seen in salivation, low arterial pressure, slow pulse, perspiration, etc. This is similar to the sleeping state, in which we also find inhibition of the higher nervous centers. (*c*) Metabolism: We have investigated mainly the metabolism of carbohydrates in schizophrenia and have found it to be very low. We have in this state a low level of the blood glucose. Carbohydrate metabolism in schizophrenia is similar to that found in hibernation. . . . When an animal is in the state of hibernation and you inject epinephrine, the state of hibernation is ended. The animal is aroused for a time. When we inject epinephrine into schizophrenics, the carbohydrate metabolism is normalized. When we inject small amounts of insulin, the schizophrenic state is accentuated. If we inject insulin into animals prone to hibernation, the animal goes deeper into a state of hibernation for one to two days. (In our work) we tend to unite these three side-effects. An animal, in his attempts to adapt to his milieu, elaborates two forms of life. One form of life is the waking state, in which we have a higher state of excitability of the nervous system. The expenditure of energy is higher. The trend of metabolism is toward a predominance of dissimilation over assimilation. In the sleeping state . . . or hibernation, we have the predominance of inhibition. Parasympathetic activity is more prominent than sympathetic, and assimilation predominates over dissimilation. When a little child [infant] is predominantly in a state of sleep, the cause of this lies in his greater need for assimilation over dissimilation. He is in a state of growth.

"These, then, are the two variants of life.

"This has its counterparts also in pathology. For example, in maniacal states (manic phase of manic-depressive psychosis) we see the tendency toward active life in exaggerated measure. In the cortex we find that disinhibition is greater than inhibition. In the vegetative nervous system we find a high blood pressure level, tachycardia, inhibition of the gastrointestinal tract, and increased metabolism. Dissimilation predominates over assimilation; therefore, manic patients lose weight. In fever states we have an analogous condition. There is marked excitability of the cortex; the patient sleeps badly, or not at all during the night. He is in a state of delirium between sleeping and waking. He loses weight. In the vegetative nervous system there is a predominance of the sympathetic over the parasympathetic. We generally find tremor, bright eyes, tachycardia, and rapid breathing.

"The counterpart (opposite) of this state with the minus sign is the schizophrenic state. It is an exaggerated passive form of life. We find inhibition, parasympathotonia, and a low level of metabolism. We see that schizophrenics are in a very poor state of nutrition; they become fat.

"All this is a general scheme. I cannot give you all the details at this time. I have an article in which I summarize our investigations, and at the end of our talk I will give you abstracts."[1]

II. Tour of Hospital

We were then taken on a tour of the hospital, which is 70 years old but looks even older. It is a large, rather shabby two-story building, built in the shape of a *U*. The base of the *U* contained the administration offices and laboratories. The two wings contained bed space for four nursing units, disturbed and quiet units for men and women. The number of patients ranged from 140 to 150 and included both voluntary and involuntary patients. All wards were securely locked, but there were no safety screens, and plenty of window glass was easily available to all patients. Despite this, Professor Popov said that glass breakage had never been a problem.

Wooden floors were present throughout. Despite the age of the hospital and a certain drabness, the rooms and corridors were scrupulously clean, and there were no offensive odors, even on the disturbed units. From the second floor, Professor Popov pointed to a small house, visible at a distance of about 300 yd. He told us that Leo Tolstoi

lived in this house for some years and during that period displayed great interest in the patients of the hospital. He requested and obtained permission to come to the hospital and talk to the patients. To make it easier for him, a small gate ("kalitka") was cut in the garden fence, which is still known as "Tolstoi's gate."

We were shown a very small (20×20 ft.) physical therapy department, which was modestly equipped with some old diathermy, galvanic, and faradic therapy apparatus. The pathology laboratory, equally small, contained an automatic slide section stainer, made in Kiev. Another, somewhat larger, laboratory was devoted to biochemistry. A small room contained a four-channel electroencephalograph, which used a shielded cage for the subject. Galvanic skin reflexes were also recorded in this laboratory. Professor Popov described some of the clinical and research applications of the latter procedure. In cases of paranoid schizophrenia with delusions of poisoning, the mention of emotionally charged subjects, such as food, would cause a marked increase in the galvanic skin reflex, whereas talking about "neutral" subjects would not cause any change in the base line. Following recovery, the patient would show a reversal of the pattern, that is, no reaction to the mention of his previous delusional material, but a normal response to other items.

Another small laboratory contained a chamber for conditioned reflex investigations, in which the subject sat in a chair attached to a cuff plethysmograph. Various colored lights and the cold pressor test were among the stimuli used. A tape recorder recorded verbal responses. Another laboratory was used exclusively for conditioned reflex experiments on the hypnotic state. Professor Popov considered the hypnotic state to have an "intermediate" quality, demonstrating "paradoxical" and "ultramaximal" responses from the standpoint of conditioned reflex theory. In certain levels of the hypnotic state a "paradoxical reaction" may be present; that is, a little stimulus may produce a great response, whereas a great stimulus may produce little or no response.

"This is the secret of the hypnotic state; that is, a little stimulus can produce a greater influence than even *unconditioned* factors. For example, a man in a hypnotic state may be able to drink bitter quinine without any reaction. This demonstrates the paradoxical dominance of feeble stimuli over stronger ones."

We were next taken into the lecture hall, which was a pleasant room of generous proportions. Its walls were covered with the portraits of the great and near-great in Russian medicine. Among those present were Pavlov, Sechenov, Balinskii, Merzheievskii, Bekhterev, Kojevnikov, Korsakov, Ganniushkin, Serbskii—and a huge bust of Lenin.

Another small library contained chiefly Russian volumes and journals, with a sprinkling of German material. No English or American journals were represented. When questioned about this, Professor Popov stated that he himself subscribes to the *American Journal of Psychiatry* and used to receive the A. M. A. Archives of Neurology and Psychiatry, the *British Journal of Mental Science*, and one or two German periodicals. He pointed out, however, that many foreign journals, including the American journals, are received regularly at the Academy of Medical Sciences and at the Lenin Library in Moscow. (I was later able to verify that the Lenin Library subscribes regularly to the *American Journal of Psychiatry*, the A. M. A. Archives of Neurology and Psychiatry, and several other American journals.) There is also an abstracting and translating service available to all psychiatrists who wish such help.

Professor Popov was asked concerning textbooks which he considered truly representative of present-day Soviet psychiatry. He listed the following three: (*a*) "Textbook of Psychiatry," by Professor Giliarovski; (*b*) "Textbook of Psychiatry," by Professor Sluchevsky, 1957, and (*c*) "Textbook of Psychiatry," by Kerbikov, Snezniewsky, Ozeretsky, and Popov, scheduled for publication toward the end of 1957.

We were then shown a small x-ray room containing rather antiquated equipment. This was apparently sufficient to provide for the resident patients. Another small room provided space for the "ambulatorium" (outpatient department), as well as an office in which to interview prospective inpatients and their families.

This small (140- to 150-bed) psychiatric hospital was staffed by 30 doctors, of whom only 6 were men. (Well over 75% of the doctors in Russia are women, and this percentage is probably higher in certain fields, including psychiatry.) The staff of 30 doctors included the research and teaching personnel, as well as those psychiatrists actively concerned with treatment. When asked to give a list of the treatments administered in his clinic, Professor Popov mentioned insulin coma therapy, prolonged sleep treatment, electroconvulsive therapy ("as a last resort"), and Aminasin (chlorpromazine) and reserpine therapy. It is worth noting that he did not mention psychotherapy. The clinic has had no experience with meprobamate.

Insulin coma therapy, following the classical Sakel method, is still used a great deal in schizophrenia. Coma lasts from 30 to 90 minutes. The period of hypoglycemia varies with the individual patient. Professor Popov believes that the effect of insulin depends on the degree of hydration and vasoconstriction. In insulin coma therapy, dehydration, acidosis, and vasodilation have the same role as they have in the epileptic state.

Despite frequent reference to work therapy in the literature, I saw little or no provision for this on the psychiatric wards we visited. Most of the patients were sitting idly on benches in the corridor, as they do in most mental hospitals all over the world, or were lying in bed. Facilities for occupational therapy were meager. There was a small showcase of spontaneous art work. It was interesting to note that in several paintings and drawings Communist symbols, e. g., hammer and sickle or red star, were quite prominent. Nowhere did I see a cross or other religious symbols, so common in such productions.

Our last stop on the tour of inspection was to the special department designed for prolonged sleep therapy. This department has a capacity of 8 to 10 beds and is equipped with special soundproofing, acoustic tile on the walls and ceiling, carpeted floors, and subdued lighting. Even the speech of attending personnel is kept low during the treatment program. (Part of this unit was still in the process of remodeling and was not in actual use during our visit.)

"Prolonged sleep treatment is used in cases of schizophrenia and neurasthenia." Professor Popov believes that prolonged narcosis is better than prolonged sleep in schizophrenia, but that prolonged narcosis is too dangerous. Therefore, prolonged sleep is used primarily in cases of neurasthenia. Sleep is used as a means of "resting" the nervous system. In the obsessive-compulsive state, the great part of the disorder (according to Pavlov) is based on a disturbance of the conditioned reflexes.

"These cases have a center with prolonged excitation in which inhibition is not possible. For example, a man walks through a city square under dangerous conditions during the civil war in the Soviet Union. He sees Red soldiers on one side and White soldiers on the other side shooting at each other. He runs through the square and arrives home safely. He has had great fear, which is natural. After several years, however, he finds that he cannot go through this square without experiencing fear. That is, he cannot inhibit the irrational fear. In such cases we use narcohypnosis with suggestion in a state of partial sleep. This treatment is also used in cases of reactive depression.

"We also have an apparatus for producing electric sleep. One can arouse the patient at any time. How does this happen? It is still not clear. There are two points of view. Electrodes are placed on the forehead and occiput, and electrical impulses occur at a frequency of 100 per second. One view is that the current which goes through the brain is the cause of the sleep. Others think that this current is too feeble to produce sleep. They think it is the rhythmic stimulation of the skin, as in Pavlov's experiments, in which a rhythmic stimulation of the same sort causes an inhibition of the

cortex, followed by radiation over the entire cortex which, in turn, produces sleep."

III. Questions and Answers

We finally finished our tour and returned to the office where Professor Popov kindly agreed to answer a number of specific questions.

Q. What is the attitude of Soviet psychiatrists to the subject of prefrontal lobotomy, leukotomy, or psychosurgery in general?

A. "We had experience, and this was not sufficient (to convince us of its merit). We have seen that we have not affected (the cases favorably) at all . . . or the effect is bad on account of the defect that it produces. The patient becomes passive. His emotional reactions become low. He is indifferent. One can understand that a man in this state is more convenient (to take care of) under home conditions. But it is not a medical (therapeutic) effect. We have (going on) a special investigation of the brains of schizophrenics, postleukotomy. The schizophrenic patients died, not as a result of the leukotomy, but from an (intercurrent) accident, some years (there) after. The entire brain (has been) investigated by Dr. Sevschenko (with special attention to the) cytoarchitectonics. The whole brain is sliced, and every 5th or 10th slice is investigated. We see (that) the damage to the brain is enormous. The operator thinks he operates on only a little part, but really the whole brain, even the occipital lobes, are involved. (In schizophrenia) we think, on the basis of Pavlov's conceptions, that the brain cells are in a very long state of inhibition and they have a possibility of recovering. The inhibited cells are without function, but they are not dead. But when the knife of the surgeon goes into the brain, the cells are dead."

Professor Popov estimated that he has seen between 40 and 50 cases of leukotomy. Between 100 and 200 cases had been operated on in the entire Soviet Union before the official ban in 1951. Professor Popov attended a special conference in Vienna in 1953 during which this subject was discussed at some length with Austrian, English, Dutch, and Soviet psychiatrists.

Q. What is your opinion as to the contributions of Freud, and what is the attitude of Soviet psychiatry to psychoanalysis?

A. "Our attitude to psychoanalysis is complete negative! (emphatically stated) We stand on the materialistic basis. Psychoanalytic measurement is not as if the mind existed in the brain, but as if the mind exists on a nonmaterial basis . . . . Freud speaks in his 'Introductory Lectures' that the nervous pathways and structure of the brain have no interest for the psychoanalyst. And we can see interesting examples (of this). Paul Schilder, as a neurologist, thinks of the brain as the basis of the symptoms. (There is) a book by Hoff and Schilder on *Lagereflexe*,[5] and in this book his thinking is materialistic and anatomically based. But this same Schilder (some years later) has a book on the psychoanalytic basis of psychoses, 'The Psychoanalytic Basis of Autismus.'* (Schilder considers that) the autismus is the result of narcissistic attitude. The libido centers more in the man than in the external world. Is *this* the explanation? Can we verify this theory?

"For example, the catatonic lies in an embryonal position. *We* (in the Soviet Union) think that it is the result of inhibition of the higher levels of the central nervous system. We give (to this catatonic patient) great doses of caffeine. Caffeine produces a prevalence of excitation over inhibition, and I see that after 10 to 20 minutes I have the effect of caffeine. I observe that the pulse becomes faster, and (shortly) afterward I see that the position is changed. He lies more like a man does usually. After an hour or so the effect vanishes. The pulse returns to its previous level, and also the patient returns to the embryonal position. From the point of view of position alone I (can) predicate the effect of caffeine. If (there is) no change, I must change my hypothesis. It was Jelliffe who said (that the) embryonal position was a picture of an experience of a new birth into the world. He (the patient) feels as if he were in the mother's uterus. How can you verify this by any arguments? This is too idealistic, taken from the context of the brain, and cannot be proved or destroyed. This means that we and the psychoanalysts do not travel on the same road."

Q. What is the essential basis for psychotherapy in the Soviet Union?

A. "Psychotherapy in the Soviet Union is based on suggestion, hypnosis, and reeducation on the rational (conscious) level. We hold consciousness (to be) more (important) than unconsciousness."

Q. Do you ever use free association in psychotherapy?

A. "Association is *facts* . . . . But the interpretation of these facts can be different. For example, we have word associations in schizophrenia. It is an old established fact that by our basis (i. e., by our reasoning) this abnormality is due to partial inhibition, and we may make a verification of this hypothesis. One of the workers gives caffeine to schizophrenics (prior to administration of a word association test). The time of reaction is smaller,

* I am unable to find such a title in Schilder's works.

and the percentage of correct associations is greater. For example, (let us say) we have 25 associations. (Prior to caffeine) 20 were incorrect; only 5 were correct. Twenty to thirty minutes after the caffeine, 20 (associations) were correct and only 5 incorrect. In doses of caffeine which are too great, ultramaximal inhibition (is produced), which is pathological. We can therefore predict the reaction. . . and verify our point of view."

Q. Can you tell us something of the training received by Soviet psychiatrists?

A. (Prior to answering this question, Professor Popov indicated that he was quite familar with psychiatric training in America and had made a careful study of Ebaugh and Rymer's book "Psychiatric Education in the United States.") "We have no special diploma for neurology or psychiatry. After six years of medical school (standard for European countries) we have three ways of teaching: (*a*) Lectures and practical work. (*b*) We have a special day when they work all day here. We have a special student circle once a week. In his free time the student goes to the clinic, works there, and has a special research project. (*c*) Works on different thema. We have a book showing the work of the students of First and Second Medical Institutes. The obligatory units (requirements?) are not so large. Each doctor must know (contribute or work on) something (which will lead to) improvement in psychiatry."

Q. The time is growing late, and I have one last question, which is also in the nature of a message from Dr. Eduardo Krapf, Chief of the Mental Health Section of the World Health Organization. Since the Soviet Union has reentered the World Health Organization, and since there is present in the world a very real need for the exchange of scientific knowledge in our field, Dr. Krapf hopes that you will avail yourself of the facilities of the World Health Organization for such an exchange.

A. "We would be glad to have exchange in science. But the psychiatrists in Switzerland did not let us join the Congress on Schizophrenia."

Dr. Ziskind (interrupting):

It will not happen again . . . .

Professor Popov (continuing):

"I am not convinced! We make a difference between the small group of organizers and the great mass of psychiatrists, who do not have a prejudged opinion. We have amical feelings to the strange (foreign) psychiatrists and (think) that they have a friendly feeling toward us. We have general goals in common to aid those who are suffering."

Our next interview was with Prof. A. R. Luria, the distinguished Soviet psychologist. We visited him in his office at the Institute of Defectology, of which he is the director. Present also was his associate, Dr. Sokolov, who is especially interested in studying the receptor systems of retarded children.

Professor Luria spoke rapid and perfect English and seemed completely at home in the language. He spoke to Dr. Gantt of the period in the late 20's when they had first met each other in Russia. "You knew me only in my 'Stone Age,'" he commented, making facetious reference to the more recent developments of his research interests.

"For the last two years or more I have been working on a new book which will be a résumé of my work of the past 20 years or so. From 1935 to 1955 I have worked almost exclusively on neurological problems, problems of neurosurgical localization, functional organization of the cortex, and psychological analysis of focal brain lesions. During this time I published a book, 'Aphasia and Rehabilitation of Brain Functions After Brain Trauma in War.' The second book will be published by Basic Books, Inc., next year, with Leontyev as co-author.

"Logically it became necessary to make *physiological-neurodynamic* analyses of normal and pathological cases. You may have wondered at the name 'Institute of Defectology.' The term 'defectology' does not exist in English. In this institute we study retarded and abnormal children, as well as those who are deaf, dumb, and blind.

"We make a *physiological* analysis of the child's general development. There are many children who cannot go to the normal school. But a simple IQ test is not enough to exclude them. There are many causes for these conditions, and we must come to a *physiological* analysis of each. First, there is the 'normal' child who hasn't acquired certain learning methods. For example, a child who loses time on account of illness and therefore has not acquired new learning methods. This is purely psychological. The problem (here) is an 'abnormal' teacher, not an abnormal child. Second, slight hardness of hearing which may be unimportant in adults, but in children it may be so important that they may not be able to form language patterns. Therefore, this group is secondary to primary receptor deficit. Third, asthenic children who are 'feeble' following general systemic illness. This type of child shows quick exhaustion. The nervous system has been affected. It shows up mainly in a difference in working ability. Fourth, mental defective, oligophrenic, and retarded morons with primary defect due to illness in the first months of development, with huge lesions in the cortex.

"The main problem is: How can we differentiate them? Formal psychological tests are not enough. We must make careful investigation into the character of higher nervous activity.

"First, we use the EEG (Dr. Novikova's department) to differentiate between focal and general symptoms. In all truly moron children we find abnormal EEG's with slow alpha rhythm. There are no such findings in the pseudooligophrenes (Groups 1 and 2).

"We also use the reactive-flicker EEG. The normal EEG reacts synchronously to an increase in frequency, but not when it is reduced. In true oligophrenia it is just the reverse. There is a book by Dr. Zislina on this subject.

"We must determine what features are characteristic of the normal and the abnormal child by the use of (*a*) general neurodynamics; (*b*) special neurodynamics, and (*c*) the role of speech in the organization of nervous activity.

"In our research methods we must always compare the formation of temporal connections with verbal reinforcement and verbal instruction. Now what exactly is the difference? In our method we use the different levels of increasing difficulty. For example, on the first level, the child is told to *press* a button on seeing the red light and *not* to press on seeing the green light. On the second level, the child is told to press on seeing the *long* green light and *not* to press on seeing the short green light. At this level the element of timing is involved. On the third level, we use the verbal negative or the mild electric shock to govern response. This is the most complex level of the three. (Professor Luria finds that both normals and morons do well on the first level, but morons find the second and third levels very difficult.)

"Professor Tepelov has found that the 'equilibrium' of a defective child is also bad. Therefore, if a defective child succeeds in forming a connection, it is then hard for him to shift. This 'inertness' is more evident in the verbal system than it is in the motor system. This 'inertness' has been studied in cases with brain lesions and also in morons. The more complex the process, the more 'inertness' is shown.

"In *every* normal situation the formation of temporal connections involves the participation of the verbal system and thereby differentiates human from animal experimentation. Speech, then, is a mode of orientation. This happens instantly in man on account of his possession of the faculty of speech. Reinforcement occurs quickly, and 'self-reinforcement' occurs only in man and not in animals. Animals require a longer period for reinforcement. In morons the verbal system does not participate because with them it is very inert.

"Now as to *technique*. How can a 2-year-old child obey the simple verbal instruction, 'If you have a light, you press'? For example, if a boy in the process of putting on his sock is suddenly told, 'Take it off!,' he nonetheless finishes putting on the sock. This illustrates an unspecific effect of speech. Therefore, the verbal system can only stimulate, but cannot inhibit."

Professor Luria went on to describe the techniques of his experiments, which were discussed in a reprint in English.[7] He concludes from his experiments that the period between the ages of 3 and 3½ is the turning point. In a 2-year-old the verbal response is weaker than the motor response. In the 3- to 3½-year-old child, however, the neurodynamics of the verbal system are superior to those of the motor system. For this reason the verbal system can be used as a regulatory apparatus.

Professor Luria then asked Dr. Sokolov to continue the discussion. Dr. Sokolov said that he was primarily interested in the study of (*a*) deficits of sensory perception, (*b*) objective study of the child's activity, (*c*) reflex organization of the perceptive processes, and (*d*) the role of perception in establishment of temporal connections for conditioned reflex formation. Three types of conditioned reflex were involved: 1. Orienting reflex: (*a*) orienting reflex as such, and (*b*) orienting reflex as behavior. This reflex could be in the motor, sensory, or vegetative system. An example of the orienting reflex was the dilation of the pupil in response to pain. 2. Adaptive reflex: (Here emphasis was placed on studying the action of the analyzer. An example of the adaptive reflex was the constriction of the pupil to light.) 3. Defense reflex: (*a*) nonspecific and (*b*) specific.

All changes of intensity of stimuli produce a change in the orienting reflex. The *interaction* of the orienting, defense, and adaptive reflexes is most important. For example, (in a classical experiment) *all* stimuli produced vasoconstriction of the finger and vasodilation of the head, at first, only as an orienting reflex. Then, after a while, the cold pressor test produced vasoconstriction of the finger and vasodilation of the head. This was cited as an example of

the method of converting the orienting to an adaptive reflex.

Dr. Sokolov then referred to the work of Dr. Granit, of Stockholm, who used subliminal light stimuli in animals, which produced no reaction. The same animals were then subjected to a very loud noise of 90 db. This produced a depressive phase, during which time the same light stimulus (previously subliminal) produced a reaction two successive times. Dr. Sokolov mentioned this work to point out the relation of the different senses to one another, which can be experimentally investigated. Dr. Sokolov added that he had studied carefully the works of the following American investigators: Brenner, Pribram, Skinner, and Lindsley.

At this point, Professor Luria agreed to answer specific questions. Since he spoke so rapidly, it was impossible to take down verbatim replies, and the following is reconstructed from rough notes taken at the time.

Q. Do clinical psychologists practice psychotherapy in the Soviet Union?

A. In the Soviet Union psychologists do *not* treat patients; only psychiatrists treat patients. Psychologists are used only in diagnosis and research, and also in the rehabilitation and treatment of brain-injured cases.

Q. Can you tell us something about psychoanalysis in the Soviet Union?

A. There is very little interest in psychoanalysis in the Soviet Union. Psychoanalysis interests itself in the depths. . . . *We* are interested in the *heights* (points finger heavenward) . . . in the nervous system of the highest type and its regulatory mechanisms.

Q. I have read that there was for a time, especially during the 20's, considerable interest in psychoanalysis in the Soviet Union. (Professor Luria himself had been on the board of editors of the *International Journal of Psychoanalysis* for a time.) Does there remain any residue of that former interest?

A. There is very little residue left. It might, however, be very good to pay some attention to investigating the mechanisms of repression, etc., but in general the ideas of Pavlov and Freud are entirely contradictory. This was discussed at length by Harry K. Wells in his second volume of "Pavlov and Freud."*

Q. In your work, what psychological tests do you find most useful?

A. We can use *any* test—but only for qualitative, and not for quantitative, analysis. We are against the use of the usual psychometrics because they are only *formal* tests and do not go deep enough. The result, or the best score achieved, means nothing. We must go deeper into the analysis of the process itself which is causing the condition. We use all the projective techniques, but not so much to determine motivation as to give us qualitative data.

Our interview with Professor Sarkisov took place in his large, pleasant, picture-lined office at the Institute of the Brain. It was by far the most impressive office we had visited. In addition to photographs of many neurologists and neuropathologists from other countries (such as Ramón y Cajal, Sir Henry Head, Babinski, Brodmann, von Economo, and many others), there were large portraits of Lenin and Stalin. When we first entered the room, Professor Sarkisov was polite but spoke in a very halting English, interspersed with long bursts of Russian. Within a few moments, after recognizing Dr. Gantt (whose name, apparently, had not registered when the appointment was first made), he suddenly opened up, broke into a warm smile with gesticulations of friendship, and his English quickly became much more fluent. On learning that I had heard several talks by his friend the late Prof. Vladimir Lebedenko, he became even more expansive and friendly. I learned later that Professor Sarkisov had worked with Professor Adrian, in England, for a year or more and had also visited the United States in 1943.

After the preliminary greetings were completed, Professor Sarkisov explained apologetically that he would have to leave shortly after noon to attend an important meeting, but he had arranged to have his various assistants explain their individual projects. In the meantime, Professor Sarkisov plunged directly into the subject of his major interest, the reticular formation of the brain.

He expressed the opinion that recent interest in the reticular formation is very

important, but thought that investigators in America, especially, have gone too far in describing its role in the subcortical connections. In this connection he expressed skepticism of Penfield's "centroencephalic" hypothesis. He felt that placing consciousness below the cerebral cortex is unwarranted.

To prove his point, he cited the following: If the reticular formation alone is cut, no changes in the EEG occur. But if the peripheral (afferent) connections are cut, then changes do occur. But afferent currents ascend via the brain stem to the medial and lateral lemnisci. If these are cut, the connections of the reticular formation are still left, enabling it to show up on the EEG on sensory stimulation. But, Professor Sarkisov added, it is completely *impossible* to cut the afferent pathways without damaging the reticular substance and vice versa.

He implied that Dr. Magoun, of the University of Southern California School of Medicine (Los Angeles) thought otherwise, and, in a half-teasing, half-serious vein, stated that Dr. Magoun had not sent him the stained preparations to show him the extent of the lesions. Professor Sarkisov stated that there is not a single cubic millimeter of brain substance which is without afferents. Dr. Ziskind promised to discuss this matter with Dr. Magoun.

He spoke of experiments designed to produce universal deafferentation in newborn cats or dogs. In such cases there are no EEG changes in the cortex on external stimulation. He promised to send reprints when the work was completed.

Professor Sarkisov went on to explain the work of the Institute in broad, general terms. The basis for all their work is morphological, and their investigations are divided into the following main groups: (*a*) Phylogenetic and ontogenetic evolution of the nervous system. (*b*) Continuation and extension of the work of Brodmann, Vogt, and von Economo on the architectonic structure of the human brain. This work, of 20 years, has already resulted in the publication of a beautiful brain atlas in 1956, a copy of which was graciously presented to each of us. (*c*) Physiological connections between the various parts of the nervous system, but always with stress on the morphology. There is much interest in extending the work of Ramón y Cajal and Lorente de Nó on the histology of neurons. (*d*) Study of axosomatic versus axodendritic connections. Professor Sarkisov has discovered that the higher one proceeds in the nervous system, the more axosomatic connections one finds *until* the cortex is reached. In the cortex the situation is reversed, and one finds more axodendritic connections. These findings were presented at the Brussels meeting last year.[9] (*e*) Biochemistry.

Professor Sarkisov has 35 scientists and 30 laboratory workers on his staff!

Dr. Adrianov then took us to the conditioned reflex laboratories. He is interested in studying the differences in the conditioned reflex response after ablation of various parts of the cortex. For example, he has found that removal of the secondary part of the cortex without the Betz cells does not disturb the conditioned reflex development.

We were shown one of the large, specially constructed rooms in which the experiments were conducted. Although the laboratories were in constant use, they were scrupulously clean. The animals appeared very well cared for, very well trained, and there were no offensive kennel odors. A dog, attached to his harness and cuff plethysmograph, remained quietly at ease as we walked in. Dr. Adrianov explained that three main methods of studying conditioned reflexes are used in this laboratory: (*a*) classical Pavlovian method, by use of the salivary fistula; (*b*) electric-shock-conditioned reflex; (*c*) free habitation, in which the dog is not harnessed but is trained (by use of food inducements) to stand on a box throughout the entire experiment. This box rests on an apparatus which is capable of registering both heavy and light movements. Visual, tactile, and

auditory stimuli are given by well-designed electronic apparatus.

Following ablation of various parts of the motor cortex, the conditioned reflexes in the dogs were lost for several months. Later, the dogs were killed, and neuropathological studies were made. Dr. Adrianov cited also the work of Prof. I. F. Popov, the physiologist who removed the neocortex and rhinencephalon in dogs. For three years thereafter the conditioned reflexes were abolished.

We were next shown the EEG laboratory by Dr. Naumova, who is working under the direction of Professor Troifimov. Her collaborators are Drs. Lubimov and Rabinovitch. The EEG laboratory is chiefly interested in studying the localization of function in chronic conditioned reflex experiments. Three new methods have been devised for the fixation of electrodes to the dog's skull. Fine spiral electrodes were applied through small trephine openings in which there was no penetration of the inner table of the skull. In some instances two electrodes went to each area—in others, six fine wires went to one area. For recording subcortical activity 17 electrodes were used. The apparatus, which appeared to be ingeniously and soundly designed, could be attached and detached from the animal with great ease, much as a complicated electronic tube with multiple connections is plugged in or unplugged from its socket.

A Kaiser eight-channel EEG apparatus, made in Denmark, was being used. The only difficulty encountered was that the writing pens would frequently come off as the result of too vigorous movements.

Our final visit was to the remarkable museum, which is under the direction of Dr. Svorikin. It was established 25 years ago and contains many excellent preparations. Since 1949, they have concentrated on preparations of the nervous system in man and lower species by demonstrating the nervous system in its relation to the whole body. The number and variety of animals were impressive and ranged from the starfish, octopus, crabs, reptiles, and birds all the way to nonhuman primates and man. The brain of an elephant was also included.

Dr. Svorikin talked a bit about Vogt, who stated that it was possible, on the basis of cytoarchitectonic studies, to differentiate the brains of criminals from those of highly trained intellectuals (such as professors) by the relative lack of inhibitory areas in the brains of criminals. Dr. Svorikin expressed some personal skepticism about the validity of this concept. He did mention that the Institute still was in the possession of Pavlov's brain, but nothing on this has as yet been published.

In Leningrad, my first interview was with Prof. P. S. Kupalov, who was kind enough to come to my hotel, since he was leaving for the week-end and would not be available during the remainder of my brief visit. Professor Kupalov, a former pupil of Pavlov, was a pleasant, mild-mannered gentleman in his middle 60's, who spoke excellent English. He had visited America and many other countries and was personally acquainted with Dr. Gantt and his work. At one time he had received assistance from the Rockefeller Foundation and was closely acquainted with the late Dr. Alan Gregg. Professor Kupalov is currently the president of the Society of Soviet Physiologists.

Since time was limited, we did not have much opportunity to discuss his work in any detail. He discussed some conditioned and unconditioned reflex experiments on the tongue of a dog which had been surgically isolated from its central nervous system connections. This work was being carried out by Dr. K. S. Abuladze in Professor Kupalov's laboratories and was reported in the abstracts of the recent Congress of Physiologists in Brussels, which had been given us in Moscow.[10]

We then talked of the experiments in sensory deprivation carried out by Hebb, Lilly, and others in America. Professor Kupalov was not familiar with this work

and asked for references, which I promised to send him.

The following morning, through the good offices of Professor Bykov, I was driven to Pavlov's old laboratories and home in Koltushi, about 35 kilometers from Leningrad, in a very rural setting. I was accompanied by Dr. M. N. Pototsky, a biologist on the staff of Professor Bykov, and our interpreter. Dr. Pototsky spoke excellent French, so that the services of the Intourist interpreter were not needed, although she continued to accompany us.

On our long drive to Koltushi, Dr. Pototsky confessed that he, as a biologist, had little or no confidence in the clinical practice of psychiatry. "It's not scientific . . . no one can check on the psychiatrist!" Shortly after making this statement, he told of one of his medical friends, a doctor whom he consults personally, who was occasionally pestered by patients who wanted to know their exact diagnosis, nature of treatment, etc., etc. When confronted by such patients, the doctor would reply to their questions by saying, "*Allez au diable!*" Dr. Pototsky, the biological scientist, defended this practice staunchly, since he said that for a patient to have too much knowledge produced too much introspection.

Dr. Pototsky expressed considerable interest in the American and English literature on psychosomatic research. Despite this, he found the papers so difficult to understand that, for the most part, the work had remained meaningless to him and to the other workers at the Institute. They had gone so far as to get expert translators and linguists from the University, but even with this aid the material remained largely incomprehensible. He had the feeling that the American and British workers were probably engaged in significant research on this problem and that there seemed to be a wealth of literature available. He expressed the hope that American workers would report their findings in simpler language, which would lend itself more readily to translation and comprehension by Russian scientists. (It seemed to me that the problem was one which was vastly more complex than that of language, and actually involved the entirely different philosophical, ideological, theoretical, and socioeconomic context in which the work was being done.)

On arriving at Koltushi, we were taken through Pavlov's laboratories by Dr. Melikova, a woman in her 50's. I was shown Professor Pavlov's study, desk, and glass-lined conservatory, filled with rubber plants, vines, and other greenery. Pavlov loved plants, and this section is kept exactly as Pavlov left it. In a nearby case is Pavlov's bicycle which he used for exercise. On the walls were photographs of Pavlov surrounded by his family of laboratory workers. One photograph showed him playing *gorodky*, a Russian game played with a stick and ball, at which Pavlov became very proficient. Nearby was the house in which Pavlov lived for many years, and which is now part of the general laboratory. I was told that future plans call for moving all the laboratories of the Pavlovian Institute of Physiology from Leningrad to the grounds at Koltushi once the proper buildings are constructed to house them. The present structures are old; heating seemed inadequate, and the only approach was by muddy dirt roads.

Dr. Melikova stated that her division of the Institute was concerned with three problems: (1) The physiology of the four types of dogs according to Pavlov: (*a*) unbalanced weak, or melancholic; (*b*) unbalanced strong, or choleric; (*c*) normal but calm, or phlegmatic; (*d*) normal but active, or sanguine. Examples of these types were shown to me. (2) Genetic considerations affecting conditioned reflexes. (3) The pharmacology of the various types.

Methods used consisted chiefly of the classical Pavlovian technique, using the salivary fistula. Other methods included the measurement of biochemical reactions, motor activity, changes in the conditioned reflexes, activity of the defensive motor reactions, and nutritive reactions. Dr. Melikova em-

phasized that they were primarily interested in the activity of the higher nervous system and not so much in activity in general.

I was next taken to the special section, in which the chimpanzees were being studied, under the direction of Dr. Leonid Firsov. Before entering the glass-enclosed building in which the huge chimpanzee cages were located, we were all asked to don white smocks. I was told that this was to prevent the expensive chimpanzees from catching a cold or upper respiratory infection from some visitor. Curiously enough, we were not provided with face masks or caps or shoe coverings, so that this procedure im-inadequate and unscientific, or, at best, as pressed me with its "token" quality as being unrealistic.

The chimpanzees, three in number, were all females, all of which were in heat. The method of experimentation differed considerably from that used in the classical procedure with dogs. No harness was used, nor were the chimpanzees attached for any length of time to a recording apparatus. Insofar as I could see, the procedure consisted of setting up various experimental conditions, with Dr. Firsov making careful observations on their behavior from the other side of the cage. He would also enter the cage from time to time to take the blood pressure and pulse with a conventional sphygmomanometer.

We then returned to Professor Bykov's laboratories in the Pavlovian Institute of Physiology in Leningrad. One of Professor Bykov's assistants, Prof. I. T. Kurtsin, discussed some of his work. He is primarily interested in chronic experiments on psychosomatic problems. In their work on peptic ulcer, they have been able to prepare dogs with two gastric pouches, one from the lesser curvature and one from the greater curvature, to study the difference in secretion between these two areas in response to conditioned reflexes. They have also worked with dogs with esophageal fistulas for sham-feeding and sham-drinking experiments. Such dogs usually require one year for preparation and are then used for several years of experimental work. Professor Kurtsin and his co-workers have discovered that it is easier to produce peptic ulcer and various other psychosomatic conditions in the "weak" type of dog and much harder to produce them in the "strong."

I was introduced to Professor Bykov in his spacious and tastefully arranged office. Professor Bykov was a distinguished-looking man in his early 60's, with graying hair and a very strong face. He apparently knew very little English or French, but spoke Russian in a slow, grave, and well-modulated voice. He inquired about Dr. Gantt, whom he had invited to speak at his Institute, and I gave him what information I had concerning Dr. Gantt's schedule. We then moved to another table in his study for coffee and cakes, and he discussed at some length, but in rather general terms, the nature of his work at the Institute. It was quite clear that Professor Bykov was deeply interested in studying the nature of psychosomatic (or, rather, "corticovisceral," as he preferred to call it) symptom formation by use of the conditioned reflex experiment.[11] In the midst of our discussion, Professor Bykov, suddenly, and without warning, announced that he would like to talk to me about another matter. He prefaced his remarks by stating that he had been for many years a pupil of Pavlov and had known him very well. For this reason he considered that he was properly prepared to correct certain misconceptions about Pavlov's life which (he felt) were current in America and which had been repeated over the Voice of America broadcasts. These misconceptions consisted of statements that Pavlov was a deeply religious man and that he was anti-Communist. This was quite contrary to the facts, Professor Bykov contended. The fact was (according to Bykov) that Pavlov did *not* believe in God, but believed only in the natural supremacy of the cerebral cortex. Therefore, he was a complete materialist. Also, he was a truly patriotic Soviet citizen and a supporter of the Com-

munist regime, which had supported him and his scientific work.

Comment

The preceding material represents a factual report of what was seen and heard concerning Soviet psychiatry during a 10-day visit to the two largest cities of Russia. It was obviously impossible to make a survey of all aspects of Soviet psychiatry during the brief time available. However, it was clearly evident to me that much more could have been seen, even within the set time limits, had the setting been anywhere except the Soviet Union. I found it extraordinarily difficult to make appointments, or to see individuals or institutions aside from those already mentioned. Not only was there the great problem of language (which was fairly well overcome by the use of an interpreter, or by the fact that most medical men spoke English, French, or German) but there was also the serious problem of communication between the representatives of Intourist and the various institutions we wanted to visit. To make matters worse, telephone directories of Moscow simply do not exist. At least there were none in the hotel, none in the rare public telephone booths, and none in the American Embassy. Apparently, the Soviet government is not too interested at the present time in improving interpersonal communications by publishing an up-to-date telephone directory.

Part of the difficulty seemed to stem from a general atmosphere of suspicion of foreign, and especially of American, visitors. This was often expressed by an attitude of defensiveness or rigid insistence on protocol. This obviously prevented the free and easy informal meetings with psychiatric colleagues which are so rewarding and so simple to arrange in other countries.

Many questions have remained unanswered. I was unable to visit a chronic psychiatric hospital, or, for that matter, to visit any hospital other than Professor Popov's clinic in Moscow. I could get no clear idea of what psychotherapy in the Soviet Union consisted—or whether private practice or private consultations still existed in some measure. What happened if a member of the Soviet elite required psychiatric attention? What kind of psychiatry actually goes on in their many outpatient clinics?

In all our interviews with the leaders of Soviet psychiatry I had the distinct impression that we were receiving something of the "party line" reply to most of our inquiries. I had hoped to sit down informally with a practicing psychiatrist who actually dealt with clinical situations in order to discuss the different ways in which we approached similar psychiatric problems. This proved to be impossible of accomplishment in the short time available—and would probably be difficult of accomplishment even if the time were doubled or tripled.

Prior to visiting Russia, I had read several articles and books in preparation. By far the most useful of these was, "Soviet Psychiatry" by Joseph Wortis, published in 1950.[12] Despite the fact that the author's Russian is limited and that he has never visited the Soviet Union, he has succeeded, on the basis of a careful review of the vast Russian scientific literature, in giving us a remarkably accurate picture. Unfortunately, the book is now considerably out of date in several areas. This is especially true in reporting the Soviet attitude toward psychosurgery, which is described as being "a well-established therapeutic procedure." Professor Luria is cited as the co-author of a paper on prefrontal leukotomy in which the results in catatonic states were considered "good" except where the picture was complicated by paranoid features. The Soviet five-year plan for medicine (1946-1950) included a program for "the surgical methods of treatment of psychoses employing not only lobotomy, but also other operations, particularly on the vegetative nervous system." However, in January, 1951, the Ministry of Health, U. S. S. R., announced that "lobotomy has been abolished by offi-

cial decree. It is theoretically incompatible with the discoveries of Pavlov."

In addition, the description of psychiatric hospital care, culled from the literature and reports of other visitors, seemed to be somewhat "rosier" than I encountered in my limited visit. Wortis writes, for example[13]:

> Segirist visited two such psychiatric hospitals in Moscow (1947) and found the atmosphere exceedingly pleasant and cheerful. The principle of the unlocked door is applied and patients have their meals in small groups at little tables. He found facilities for electro- and hydrotherapy, continuous narcosis treatment, and especially for occupational therapy.

I saw no facilities for hydrotherapy. The facilities for occupational therapy were minimal, and I did not consider the atmosphere particularly pleasant or cheerful. These, however, are very minor criticisms of a book which has succeeded remarkably well in presenting the essence and spirit of Soviet psychiatry.

Early in his book, Wortis states:[12]

> Soviet psychiatry can best be understood if it is related to three basic sources of influence: (*a*) its socialist setting in a broad framework of public health services; (*b*) its conformity with the general principles of dialectical materialism; and (*c*) the teachings of Pavlov.

The accuracy of this observation was completely borne out by my experience. Even a casual reading of the factual report demonstrates the enormous influence of Pavlov and the importance of the strictly materialist approach in Soviet psychiatry.

My own impression was that Pavlovianism, despite its refinement and expansion, had now become a constricting influence on Soviet psychiatry and psychiatric research. I was struck, for example, by the strong contrast which existed between their psychiatry, on the one hand, which denied the influence of "unconscious factors," and the realities of their political life, on the other hand, in which the shrewd interpretation of external behavior based on a deep understanding of the importance of "unconscious factors" often meant the difference between success or failure, freedom or imprisonment, life or death.

The American psychiatrist may find himself in a curious position regarding Soviet psychiatry. He may approve wholeheartedly of certain features, and condemn others, depending, of course, on his own special orientation. The orthodox psychoanalyst will probably applaud the Soviet ban on prefrontal lobotomy, at the same time that he condemns the wholesale rejection of Freudian theory. The conservative eclectric who applauds the Soviet use of electroshock therapy "as a last resort" may question seriously their free use of other somatic therapies. The American organicist who approves wholeheartedly the materialistic approach will probably refuse to be confined by Pavlovian concepts. Paradoxically enough, it appears that the Soviet approach to psychiatry is an ultraconservative approach. To cite only one example, the two treatment methods in American psychiatry which lie at extreme opposite poles, namely, prefrontal lobotomy and psychoanalysis, are either officially banned or unofficially condemned—leaving only the large middle ground, with its emphasis on physiological considerations.

Soviet psychiatry, unlike European psychiatry, is not "hospital-oriented." There was much more emphasis on outpatient treatment and prophylaxis than there was on hospital-building programs.

The average Soviet psychiatrist, in spite of, or possibly because of (?), his less formal training, is much more research-oriented than his American counterpart. One practical reason for this is that research is encouraged and rewarded in the Soviet Union and provides a very attractive route for rapid advancement in position, prestige, and salary.

Wherever I went, it was obvious that the Soviet psychiatrists were far better informed on what was going on in American psychiatry than the reverse. There is a tremendous thirst for knowledge, and the Soviets have become a nation of voracious readers. The reading rooms of the massive Lenin Library in Moscow were filled from morning to

night with serious readers. Bookstores are constantly filled with purchasers. Editions of medical and technical books are quickly exhausted. Despite the freely admitted difference of viewpoint, there seemed to be a genuine interest in establishing greater exchange of scientific data.

The lack of communication which has existed for so many years between the two countries has given rise to many misconceptions and distortions on both sides. A leading Soviet psychiatrist,[14] who visited the United States for the first time in 1958, admitted openly that he had entertained many wrong ideas about America, American psychiatrists, and American psychiatry—and that he was glad to see with his own eyes that he had been misinformed. He was particularly impressed by the serious interest of American psychiatrists in the scientific approach to psychiatry, by their friendliness, and by their open-mindedness. In this case, one visit was more effective than reading 100 papers.

There is now a pressing need for level-headed appraisals of each country's methods and achievements in the field of psychiatry. It is hoped that the doors of communication will remain open for a long time, for we have a great deal to learn from each other.

1712 Rhode Island Ave. N. W. (6).

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An Investigation of Anxiety as Related to Guilt and Shame

MELVIN PERLMAN, Ph.D., Downey, Ill.

In the past, while many sources of anxiety were recognized, the resulting anxiety was always considered as a unitary concept, i. e., as having the same psychological and physiological correlates regardless of etiology. The validity of this implicit working hypothesis has seldom been challenged. However, in recent studies[2,3] investigating anxiety in paratroopers in training, differences in the types of anxiety elicited were noticed. These differences could be accounted for, in part, by postulating the existence of two distinct types of anxiety, one related to shame, and called "shame-anxiety," the other to guilt, and called "guilt-anxiety." This differentiation of types of anxiety was first fully elaborated in papers by Alexander[1] and Piers.[8]

The three terms to be dealt with in this paper, anxiety, guilt, and shame, are defined as follows:

Anxiety: "A conscious experience of tension [apprehension, dread or foreboding] which is related to apprehension cued off by a threat to some value which the individual holds essential to his existence as a personality."[7]

Guilt: The result of a conflict between the ego and the superego; an internal tension generated by the transgression of the barrier or boundary erected by the superego (conscience, ethics, or moral code); these transgressions are usually, but not necessarily, aggressive or sexual impulses which are not acceptable to an internalized punishing image. In more general terms, guilt may be considered to arise whenever an individual becomes aware, either consciously or unconsciously, of doing something, or of an impulse to do something, which is not acceptable to, or violates the precepts of conscience.

Shame: The result of a conflict between the ego and the ego ideal; an internal tension which is generated by not reaching a goal; failure of an individual to actualize or approach his ego ideal (desired social role). In more general terms, shame may be considered to arise whenever an individual fails to meet external standards set by those whom the individual wants to please, or may be the failure, or threat of failure, to reach a goal set by the individual's desired concept of himself.

It will be noted that in this study we are interested in what has been called "free anxiety,"[3] and are not concerned with "bound anxiety." "Bound anxiety" is usually considered as a construct which accounts for the energy underlying a symptom complex, and thus not amenable to overt measurement. "Free anxiety" is anxiety which is subjectively experienced as an internal dread, fear, or apprehension and is usually accompanied by some physiological expression of anxiety, such as tenseness, restlessness, sweating, tremor, palpitation, etc.

From the dynamics of guilt and shame, it appears that these two affects can have opposite effects upon behavior. "Guilt-engendered activity is at best *restitution* (sacrifice, propitiation, atonement) which rarely frees, but brings with it resentment and frustration rage which in turn feed

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new guilt into the system."[10] Shame-engendered activity, on the other hand, is seen in ambitious drive directed at the lessening of feelings of inferiority and inadequacy through identification, and if coupled with creativeness "may actually lead to a spontaneous curing of the original narcissistic wound, . . . Whereas the shame-driven might be propelled beyond his natural limitations and break, the guilt-ridden as a rule will not even reach his potentialities."[11]

It can further be shown that individuals, in terms of their earlier experiences, may be differentially predisposed to react to guilt-provoking and shame-provoking experiences. We may thus speak of guilt-prone and shame-prone individuals. This is not meant to delineate or to imply a dichotomized typology. Rather, such a statement is aimed at postulating that there may exist two separate continua, with individuals identified as being located somewhere along each. Only in terms of relative proneness toward one or the other of these affects may we identify persons as being guilt-prone or shame-prone.

In a like manner, we may be able to delineate certain situations as being either shame-provoking or guilt-provoking stresses, the former being a stress related to not living up to an ideal, the latter being related to some threat of violation of conscience.

Several hypotheses related to the above theory were tested.

1. In a shame-stress situation, shame-anxiety will increase more than guilt-anxiety.

2. Persons who are identified as relatively shame-prone will report themselves as more concerned (anxious) about specific situations involving the threat of evaluation (such as examinations) than will persons identified as guilt-prone.

3. Shame-prone persons will be observed as more anxious about such evaluation procedures than will guilt-prone persons.

4. Shame-prone persons will identify their most anxious experiences as being related to shame-type stresses rather than to guilt-type stresses, as will be the case for guilt-prone persons.

5. A shame-type stress will differentially affect shame-prone and guilt-prone persons.

Procedure

Since none of the published paper-and-pencil tests of personality had attempted to differentiate these two types of anxiety, it was necessary to obtain some objective measure of guilt- and shame-anxiety in order to investigate the hypotheses in this study. The Anxiety Attitude Survey (AAS) was devised as an objective measure of both the relative proneness to guilt- and shame-anxiety and the momentary level of anxiety as related to shame and guilt. The AAS consists of 54 statements of the type, "John cheats on an examination" and "A young man finds out he has impregnated his girl-friend." The subject is asked to rate along a nine-point scale "how anxious he feels most people would be were this to happen to them." Scoring of the AAS yielded four separate but nonindependent scores. The two basic scores are the G score (total of ratings on 26 guilt items) and the S score (total of ratings on 26 shame items). In addition, there was the A score, which was obtained from the sum of G and S scores and represented total anxiety irrespective of type, and the Guilt minus Shame (G—S) score, obtained from the difference between the number of shame items and the number of guilt items the subject rated above the value of his own median rating. The G—S score was used as a measure of relative guilt- or shame-proneness, minimizing the effect of response tendency in interindividual comparisons. Both the reliability and the validity of the AAS scores were explored.*

The AAS was administered to a group of 63 male first-year medical students on two separate occasions, once near the beginning of a school term and later, as near as possible to the final examination period, a period construed as a natural shame-provoking stress situation. In addition, the subjects were also administered the Mandler and Sarason "Questionnaire on Attitudes Toward Three Types of Testing Situations,"[6] were asked to rate

* The AAS was administered to a group of 64 male college students on two separate occasions. Estimates of reliability were based on a combined internal consistency and test-retest method and yielded coefficients of 0.80, 0.83 and 0.35 for the G score, S score and G-S scores, respectively. Test-retest reliability of the A score was 0.71. Face validity of the items was provided by using only those items on which 3 training psychoanalysts and a majority of 11 clinicians agreed reflected the definitions of shame and guilt.

their classmates on anxiety about the coming examinations, and were asked to answer two questions aimed at identifying the type of stress to which they were most vulnerable. The "questionnaire" was used as an independent measure of the subjects' vulnerability to evaluation procedure anxiety (a shame stress). The questions used were designed to assess, in an approximate manner, the relative stability of shame- and guilt-proneness.

Analysis of the data was considered from three frames of reference: results for the total group, results for a criterion group, and qualitative results from intensive study of six selected subjects. The criterion group was composed of 23 subjects whose scores on the AAS placed them in the upper and the lower 20% of the total sample on relative guilt- and shame-proneness. The six subjects studied intensively were selected on the basis of being at the extreme ends of the score continuum on the AAS. They represented the three subjects most shame-prone and the three most guilt-prone who volunteered for further participation. No attempt was made to compare these six subjects quantitatively. Instead, all of the individual data, Rorschach Test, Thematic Apperception Test, Forer Sentence Completion Test, and the interview materials, were analyzed in a case-study manner by the experimenter and two experienced clinical psychologists† with the explicit aim of more clearly delineating the personality dynamics of each subject and qualitatively exploring the similarities and contrasts of the two types of subjects.

Results

Evaluation of the results of this study is contingent upon two factors: the adequacy of the AAS and the adequacy of the stress situation. The AAS and the several scores derived from it have been found to be reliable at the 0.80 level or better, a level which seems to be adequate for most experimental procedures. The validity of the AAS and its scores is not so patently answered. The AAS was constructed on the basis of face validity. It includes only items which 3 training psychoanalysts‡ and a majority of 11 other trained clinicians agreed related to the definition of either shame or guilt. No statistical evidence could be obtained relative to whether subjects' scores on the AAS were reflective of their predilections or proneness to guilt or shame, but examination of the results from the intensive study of six selected subjects (see below) suggests that the AAS is able to identify persons whose relative vulnerability to guilt-anxiety and shame-anxiety (as defined herein) is different.

The adequacy of the stress situation, however, left much to be desired. That the final examination period was a period of much concern and anxiety for the subjects was amply attested to by spontaneous comments of the subjects. They were extremely concerned about all of their examinations and realized that failure could result in either repeating a course, and thus being delayed a full year in their progress toward their goal, or in being unable to continue in this medical school. Failure of this latter type would constitute a severe blow to the subject's self-esteem and probably necessitate a complete change of goals. However, because of the subjects' school schedule, they were only available for testing one full week prior to their first "big" examination. We might thus assume that the general level of anxiety for the entire group had not been raised to the maximal point that would be expected had they been able to be tested immediately prior to their first examination. This assumption is supported to some degree by the subjects' spontaneous comments at the time of the second testing that they were not very "spastic"§ as yet. Results are thus interpreted from the standpoint that only minimum, though meaningful, stress had been achieved.

While the first hypothesis led to an expectation that shame-anxiety would increase more than guilt-anxiety, this did not occur. On the contrary, the means of all scores decreased. In addition, the S scores decreased more than the G scores, though this difference was not significant. (The mean

† Drs. Sheldon J. Korchin and Hedda Bolgar analyzed in a case-study manner the protocols of all six subjects.

‡ Drs. Roy R. Grinker, Gerhart Piers, and Charlotte Babcock cooperated in this phase of the research.

§ "Spastic" is a term used by these medical students to describe the anxiety they experience before an examination.

difference of the S scores was −4.60; that for the G score, −2.57. Standard errors of the differences were 2.53 and 2.09, respectively.) This same lack of significant differences was found in the criterion group. Thus, in the present experimental situation this hypothesis was not substantiated.

It was hypothesized that shame-prone persons would report themselves as more anxious about examinations than guilt-prone persons. The Mandler and Sarason "questionnaire" was used as the measure of reported examination anxiety, and it was expected that there would be a strong positive relationship between scores on this questionnaire and the shame score (S) of the AAS. Contrariwise, a negative relationship with the guilt score (G) was expected. When the subjects were divided into a high-anxious group and a low-anxious group in accordance with the procedure of Mandler and Sarason and the scores on the AAS dichotomized at the median value of the scores for each subgroup, it was possible to check the relationships by use of the "exact treatment of 2×2 tables."[4] None of the relationships approached significance, thus failing to support the second hypothesis. The same lack of relationship was found in the criterion group and in the total group when a later correlational analysis was performed. The correlation coefficients between the several AAS scores and the "questionnaire" scores ranged between +0.04 and −0.11.

In order to investigate the relationship between overt, observable anxiety related to the stress situation and the several types of anxiety as measured by the AAS, each subject was asked to identify the five classmates he felt were most and least anxious about the coming examinations. After ruling out the effect of relative social isolation and eliminating from statistical consideration all subjects rated by less than five of their peers, ratings of anxiety were translated into scores and the 32 subjects remaining were divided into two subgroups: high-anxious and low-anxious. Scores of these subjects on the AAS were compared, and it was found that there was a significant relationship ($P=0.027$) between overt anxiety and A_2 (total A score on second administration), S_2 (shame-anxiety score on second administration) and G_{diff} (positive or less negative differences between scores on first and second administration on guilt score). A less significant relationship ($P=0.077$) was found for A_{diff}, G_2, and S_1 (Table 1).

TABLE 1.—*Probability Values of Relationship Between Ratings of Anxiety by Peers and Scores on Anxiety Attitude Survey (AAS)* (N=32)

Variable	*P*-value *
A (first administration)	0.204
A (second administration)	0.027
A differences (A_1-A_2)	0.077
G (first administration)	0.204
G (second administration)	0.077
G differences (G_1-G_2)	0.027
S (first administration)	0.077
S (second administration)	0.027
S differences (S_1-S_2)	0.204
G-S (first administration)	>0.300
G-S (second administration)	>0.300
Mandler and Sarason Questionnaire	0.007

* Value of *P* obtained from the "exact treatment of 2×2 tables,"[4] using one-tailed hypothesis.

These relationships are not independent, since A is the sum of G and S. Thus, the significant relationship between overt anxiety and A_2 is probably a function of the increase in S_2 and G_2. Even so, these results tend to indicate that those persons who are seen as most anxious by their peers, or, in more general terms, those who show overt signs of being anxious about a coming examination, tend to have a less pronounced decrease in the anxiety they project onto an anxiety questionnaire.

The rating of anxiety by peers was also found to be significantly related to scores on the Mandler and Sarason questionnaire ($P=0.007$). Part of the explanation for this relationship lies in the fact that many of the items in this questionnaire ask the subject to rate himself on such overt signs of anxiety as perspiration, uneasiness, and

confidence before, during, and after examinations. These are probably the very things on which peers based their ratings of anxiety.

In order to investigate the relative stability of proneness to guilt and shame, the answers of the criterion group to the question asking for their most anxiety-provoking experience were categorized as either guilt-type or shame-type stress in line with the definitions and the types of situations set forth in the AAS. Only 17 of this group's answers could be categorized. For these, however, the shame-prone persons tended to give shame stresses more frequently than the guilt-prone or vice versa ($P=0.110$). These results tend to support the relative stability of these modal personality orientations, though at a low level of significance.

The differential effect of the shame stress on the guilt-prone and shame-prone subjects was investigated through an analysis of the changes in the criterion group's scores between the first and the second administration of the AAS. Since we are dealing, in this instance, with extreme groups, we would expect that retest scores would be affected by regression toward the mean, and it was thus necessary to partial out this effect. Analysis of the data showed that the changes found could be accounted for by regression toward the mean. In other words, there was no significant change in emphasis in reported guilt-anxiety and shame-anxiety under the mild stress conditions for persons in the criterion group. This is not to say that no change was found. The changes found were not large enough to be statistically significant at the 5% level ($\chi^2=5.27$; $d.\ f.=2$), but did point to an interesting pattern or trend of change.

The techniques used for testing the changes in emphasis involved the use of a "sign test," based upon whether the subjects' scores in each subgroup fell above or below the mean score of each subgroup expected on the basis of regression toward the mean. Chance expectation was that 50% of each subgroup would fall above and 50% below the regressed mean of the subgroup. Actual findings were that only 3 of the 11 guilt-prone and 3 of the 12 shame-prone subjects fell above the expected mean values (Table 2). With the two groups combined, this meant that 74% of the criterion group fell below values expected by chance. In other words, while not significant, there was a strong trend for the extreme groups to evidence a relative increase in shame-anxiety under a mild shame stress.

TABLE 2.—*Relative Increase in Shame-Anxiety (Decrease in G-S Score) for Criterion Group*

Group	Above Expected Mean *	Below Expected Mean *
Guilt-prone	3	8
Shame-prone	3	9

* Predicted means obtained by use of regression of $(G_1 - S_1)$ on $(G_2 - S_2)$ separately for each subgroup.

In the intensive study of six selected subjects from the extreme groups, there were many similarities, especially in relation to intellectual ability. While all six subjects were in the bright average to superior range of intelligence, intellectual constriction and stereotypy were evidenced in all of their records. However, one difference between these two groups stood out in a pronounced way. This difference was found in what was conceived as the area of central conflict, or central problem for the subject. For the guilt-prone subjects, the central problem was one of *aggression and its control*, though the subjects handled this problem in different manners; i. e., they capitalized on different defenses. For two of them control was rigid and resulted in what may be considered subclinical depression. For the third guilt-prone subject there was a marked tendency toward the use of paranoid projective defenses. In all three of these subjects, the competition found in their scholastic endeavors could well be considered a sublimated, more socially acceptable form of aggressivity.

In contrast to the guilt-prone persons, the central problem for all three of the shame-prone persons was one of *adequacy versus inadequacy*. Psychologically speaking, they all seemed to be asking themselves the question, "Who am I?" Two of them could be considered subclinical inadequate personalities; the third, close to a clinical case of obsessive-compulsive neurosis. The competitiveness, or, rather, the desires for scholastic achievement, on the part of these three subjects can be seen as a means of attaining much sought-after love and recognition. In discussing these six subjects, it is important to remember that they are all functioning members of society. However, even casual inspection of the psychological test materials for these subjects reveals that they do represent extremes of what would be considered a "normal" population.

Comment

Results of this study seem to substantiate the theoretical distinction between guilt-anxiety and shame-anxiety. However, in the experimental attempt to stimulate increases in shame-anxiety, results were not clear-cut. Of the several factors which may have contributed to this failure, the most prominent seems to be the mildness of the shame-stress situation.

The moderate, but insignificant, decrease in anxiety can be interpreted as a result of increased defensiveness under a mild stress situation. This would be consistent with the theory that anxiety serves as a warning signal (at the lower levels of intensity) and primarily tends to increase the subject's "vigilance." With such a heightened state of vigilance, the need to deny feelings of anxiety becomes increasingly important to the maintenance of integrity. However, since it was found that persons who were seen by peers as being most anxious, had less significant decreases in anxiety scores, it may mean that those subjects who experience the greatest degree of stress over and above their initial, chronic level, were no longer able to continue this defense to maximum advantage, and thus were unable to decrease effectively the anxiety projected onto the AAS.

In addition, it was noted that in the extreme group of guilt- and shame-proneness, there was a strong (but statistically insignificant) over-all trend toward a relative increase in shame-anxiety under the mild shame stress. Since there was no such trend evidenced for the total group, this may suggest a direct relationship between extremeness of guilt- or shame-proneness and relative vulnerability to stress. Since the six selected subjects who represented the extremes of guilt-proneness and shame-proneness were seen as representing levels of psychopathology barely within the normal range, parallel findings for the remainder of the criterion group would suggest a strong relationship between pathology and vulnerability to anxiety under stress. While these latter statements are purely conjectural, they may point the way to further research on this problem.

While both the AAS and the Mandler and Sarason "Questionnaire on Attitudes Toward Three Types of Testing Situations" were related to overt, observable anxiety, as reported by peers, they were not related to each other. The differing structure of the two tests may contribute to the lack of relationship between these two, since on one, the AAS, the subject is asked to rate his opinions of others, and thus only projectively himself, and on the "questionnaire" the subject is asked to rate himself. This may have led to differential defensiveness in the two tasks, but this effect has to be conjectural.

In light of the relationship of these two instruments to overt anxiety, two further post hoc hypotheses concerning their lack of relation to each other can be suggested. One is that the AAS deals with a broader spectrum of situations precipitating anxiety, whereas the Mandler and Sarason "questionnaire" deals exclusively with manifest anxiety as experienced by the subject before, during, and after examinations. The other

hypothesis is that the AAS may be tapping a different layer of personality than the "questionnaire," the latter dealing with superficial feelings of anxiety and tenseness, the AAS dealing more with the underlying taboos and barriers which the individual must constantly defend himself against, even in some instances to the extent that the demonstration of overt anxiety may have negative value for the person.

Guilt-anxiety seems to be a real phenomenon, distinct from shame-anxiety, and has to be taken into account in any attempt to understand personality. The marked consistency found in the intensive evaluation of the six subjects who represented the extremes of guilt-proneness and shame-proneness illustrates the sharp differences in the personality structure of these persons. Although there were only three cases of each type, the homogeneity of central problem for the two types of persons bears out much of the formulations of Piers. It thus becomes important in therapy for the therapist to attempt to discover whether the basic character structure of the patient is one in which there is an excessively strong superego that is causing the patient's anxiety, or whether the patient feels anxious about his inadequacies in reaching his goals.

The results of this study are suggestive of some of the basic differences that obtain between guilt and shame and their relation to anxiety. However, we have dealt here only with a shame-type stress. Further research on persons differentially predisposed toward guilt- or shame-anxiety when subjected to a guilt-type stress would allow us further amplification of these differences. Even though further research is now being carried on in order to allow clearer differentiation of guilt- and shame-prone persons, the intensive study of six subjects seems to bear out the validity of the AAS for isolating or identifying the basic character structure of individuals.

Summary

The Anxiety Attitude Survey (AAS) was devised as an objective measure of both the relative proneness to guilt- and shame-anxiety and the momentary level of anxiety as related to guilt and shame. The AAS was administered to a group of 63 male medical students on two separate occasions, the latter during a period construed as a shame-stress situation. They were also given the Mandler and Sarason "Questionnaire on Attitudes Toward Three Types of Testing Situations," were asked to rate their classmates on anxiety about coming examinations, and were asked to answer questions identifying the type of stress to which they were most vulnerable. In addition, six subjects rated as most guilt-prone or shame-prone were studied intensively.

No relationship was found between guilt- and/or shame-anxiety and anxiety about examinations. There was a mild decrease in total anxiety for the entire group, with a moderate increase in shame-anxiety for those subjects showing the greatest proneness toward guilt- or shame-anxiety. The intensive study of six subjects demonstrated a decided difference in the basic character structure of guilt-prone and shame-prone subjects with a high degree of consistency. The central problem for guilt-prone persons seems to be a problem of control over the expression of aggressive impulses; the central problem for shame-prone persons seems to be a problem of adequacy versus inadequacy. The consistency found in these subjects was offered as evidence to support not only the theoretical hypotheses concerning these two affects but also the validity of the AAS's ability to isolate or identify guilt-prone and shame-prone persons, at least at the extreme values. Suggestions for further research and possible implications on personality theory and therapy are made.

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What Is the Nature of Psychomotor Epilepsy?

EDWARD L. PINNEY Jr., M.D., Brooklyn

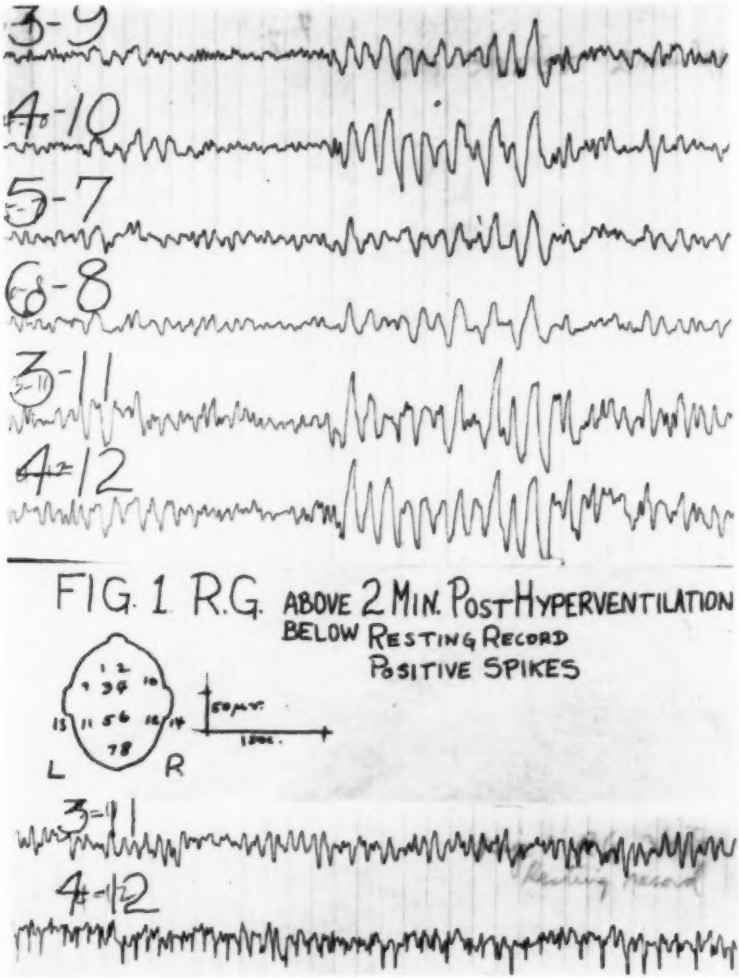
The study of a case from a family with four generations of abnormal behavior but with no convulsions is presented.

Accepted for publication March 25, 1958.

From the Brooklyn State Hospital, 681 Clarkson Ave. (3).

Report of Case

R. G., a 41-year-old married white man, was admitted to the Brooklyn State Hospital on March 4, 1955, with a history of "something like a brain attack." It was said that "he feels well for a while, then has an attack."



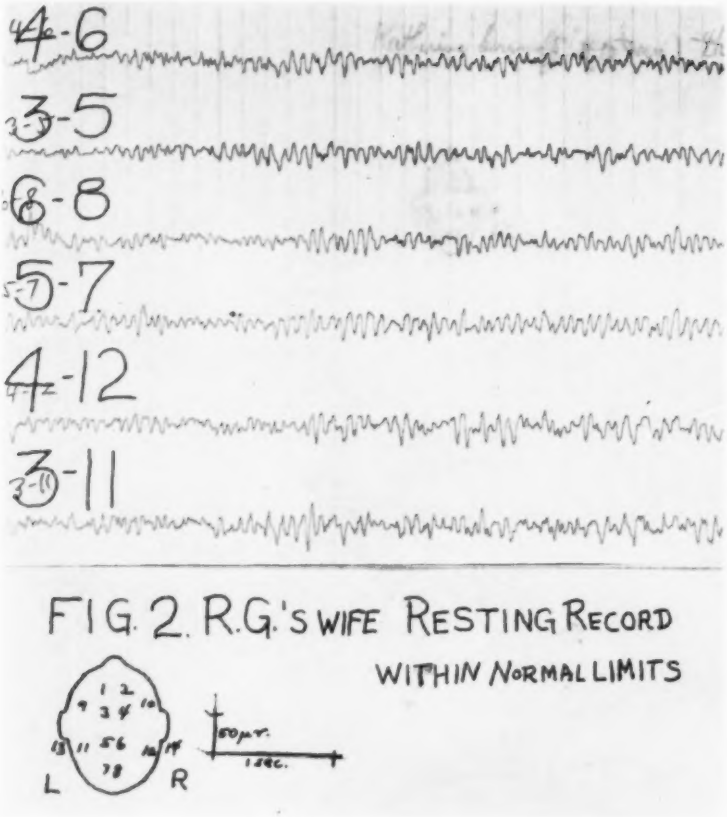


FIG. 2. R.G.'s WIFE RESTING RECORD WITHIN NORMAL LIMITS

He had gone to Florida the previous January because he wanted to try out a system for winning at horse racing. He became irrational and hyperactive at his hotel and had to be hospitalized. Subsequently, he was returned to New York to a receiving hospital and transferred to Brooklyn State Hospital. He claimed amnesia for a great part of the weeks in Florida and his behavior prior to admission to Brooklyn State Hospital.

He had been previously hospitalized at Brooklyn State Hospital on Jan. 30, 1953. At that time it was noted: "There is a history of a vague and confused episode of excitement, during which time the patient talked irrationally, became disturbed, and shouted without provocation, and was somewhat boastful and grandiose, with some degree of confusion. On the other hand, he denied having paranoid delusions, hallucinations, or other abnormal trends. He was sensorially clear." At diagnostic conference it was stated that "diagnosis is not clear"; however, his condition was diagnosed as manic-depressive psychosis, manic type. He was released on July 1, 1953.

He had completed 10 grades of school, leaving to go to work at the age of 14 years. He was a major contributor to the support of the family as soon as he was able to work. His father had been incompetent to support the family. The patient had married and had three children, had worked steadily, and had been considered of normal mental standard.

His first hospitalization had occurred after he had had a mild head injury at work. He had not been unconscious. Apparently he had suffered only a scalp laceration. Neurologic examination showed no abnormality. His behavior six days after the injury was bizarre and led to his psychiatric hospitalization.

The family history revealed that his father, E. G., had been hospitalized at Brooklyn State Hospital on Sept. 9, 1941, and that the latter's father (R. G.'s grandfather) had died at Brooklyn State Hospital in 1916. E. G. had been the youngest of 10 children. Three sisters of E. G. (R. G.'s paternal aunts) and a brother (R. G.'s uncle) had died in state mental hospitals. A son (R. G.'s brother)

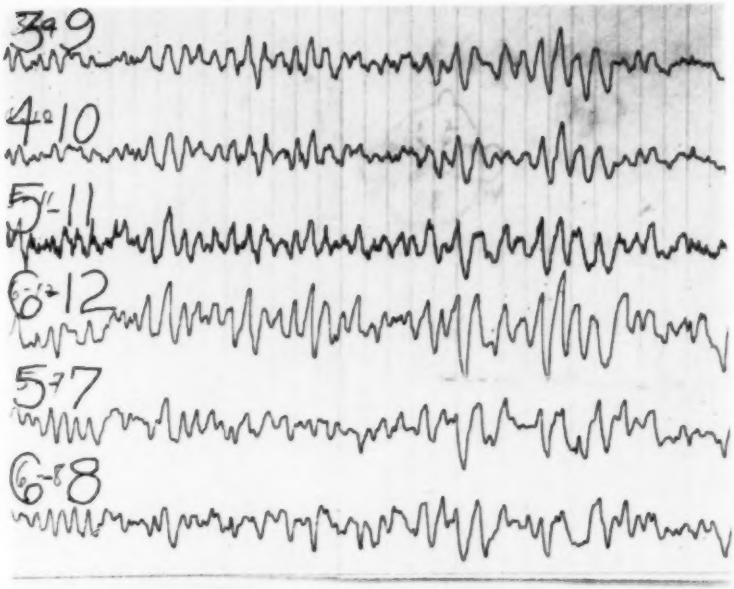
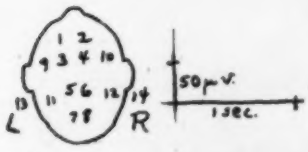


FIG. 3. R.G., JR. HYPERVENTILATION RECORD



had been hospitalized for a mental disorder in another state. There are five other children (R. G.'s siblings), who have not been hospitalized. R. G.'s three children will be discussed below.

E. G. (R. G.'s father) had first been hospitalized for about one month in 1924. At that time it was said that four years previously he had had a "slight nervous breakdown" lasting three months, during which there was nothing very abnormal except that he "talked a lot about religion." This places E. G.'s first known episode at 20 years of age. On his later admissions (1941, 1945, 1946, and 1949) the statement was made that "he has 'spells' about every five years, when he acts very peculiarly. During this time he also drinks heavily. During these spells he talks a great deal, does very odd things, such as moving things about in the cellar so that it cannot be entered, and is very active both in politics and in religious activities, although when he is not in 'one of his spells' he is not interested in either." He also ate odd mixtures of food.

Neurologic examination was negative. There was no history of convulsions. He had been unconscious for several hours in 1915 from a head injury sustained while diving.

Because of the history of head injury, an electroencephalogram was made soon (March 22, 1955) after R. G.'s admission. This record showed (Fig. 1) an alpha pattern of 9 per second, well sustained, with paroxysmal bursts of high-voltage 6- to 7-per-second activity, lasting one to two and one-half seconds. In one part of the resting record a series of positive spikes in the frequency of 6 to 7 per second appeared in the right-motor to the right-posterior-temporal combination. This finding was consistent with psychomotor epilepsy.

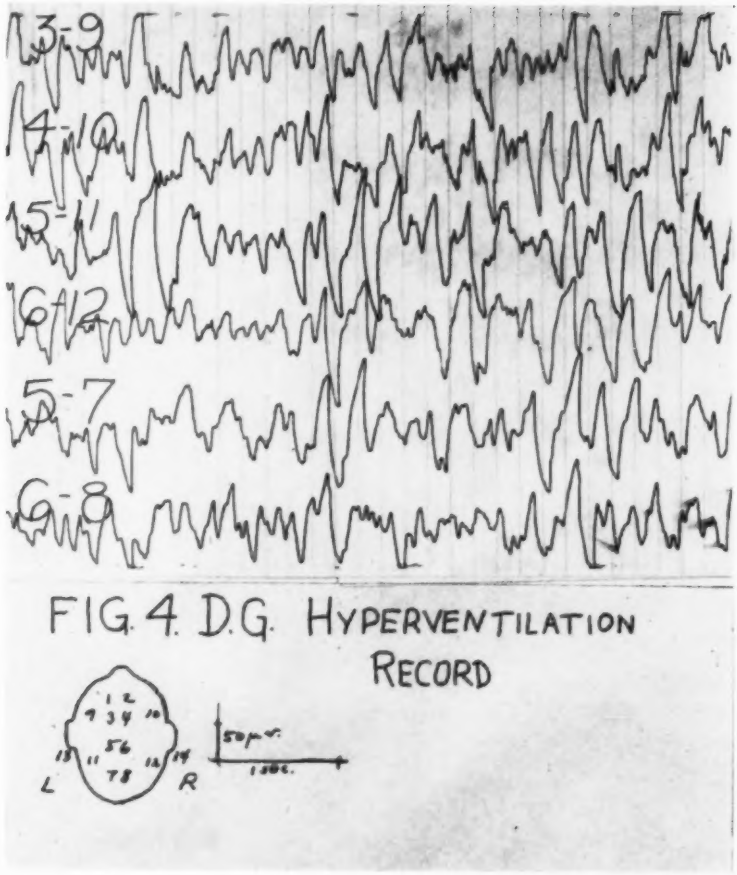


FIG. 4. D.G. HYPERVENTILATION RECORD

As a result of the EEG findings, R. G. was given diphenylhydantoin (Dilantin) sodium 0.1 gm. t. i. d., and repeat EEG studies were done. There was a diminution in frequency and amplitude of the bursts of paroxysmal dysrhythmia, but the abnormal pattern persisted.

His behavior improved. He was calmer, more cooperative, and not so inclined to make a joke of everything. He did not like this change and complained that "the medicine keeps me from getting happy."

The family history suggested that electroencephalographic studies on the others were desirable, and these were done.

R. G.'s wife had a record (April 22, 1955) within normal limits (Fig. 2). Their three sons: R. G. Jr., aged 16 years; D. G., aged 9½ years, and K. G., aged 7 years, showed grossly abnormal records (April 3, 1955) with a psychomotor pattern (Figs. 3, 4, and 5). Clinically, they had had difficulty in school. This was attributed to strictness of the nuns in parochial schools which they had attended. The oldest of the three had been involved in delinquent acts but had escaped arrest.

An EEG study (May 9, 1955) on E. G. (R. G.'s father) at the age of 65 years, revealed a well-sustained alpha pattern of 8- to 8½-per-second frequency and of relatively low amplitude, with much beta activity (Fig. 6). It was within the outer limits of normal. R. G.'s brother, E. G. Jr., aged 27, had an EEG study (April 9, 1955), revealing a fairly well-sustained alpha pattern of 9½ per second with a voltage of 25μv. to 50μv.; however, on hyperventilation there were short (one-second) bursts of 7-per-second, high-voltage activity (Fig. 7). EEG studies on R. G.'s five other siblings were done and were not remarkable. No one in this family has a history of convulsions.

In R. G., his children, and E. G. Jr., the EEG changes suggest a strong hereditary

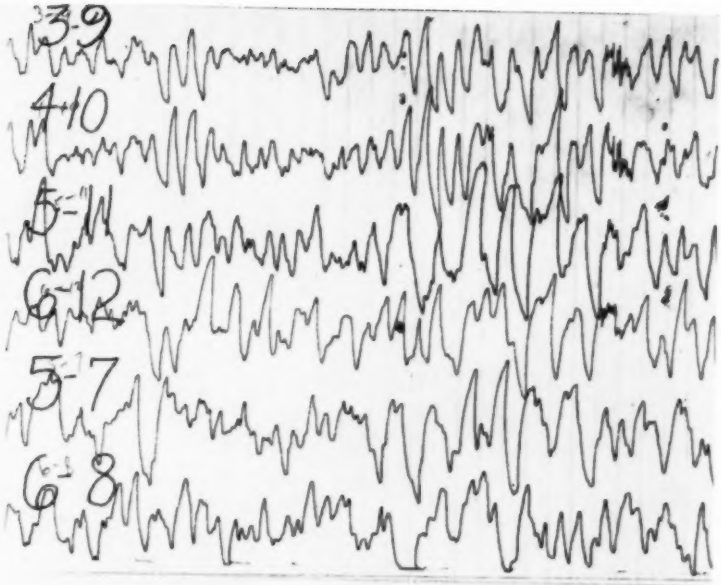
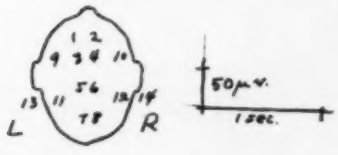


FIG. 5. K.G. HYPERVENTILATION RECORD



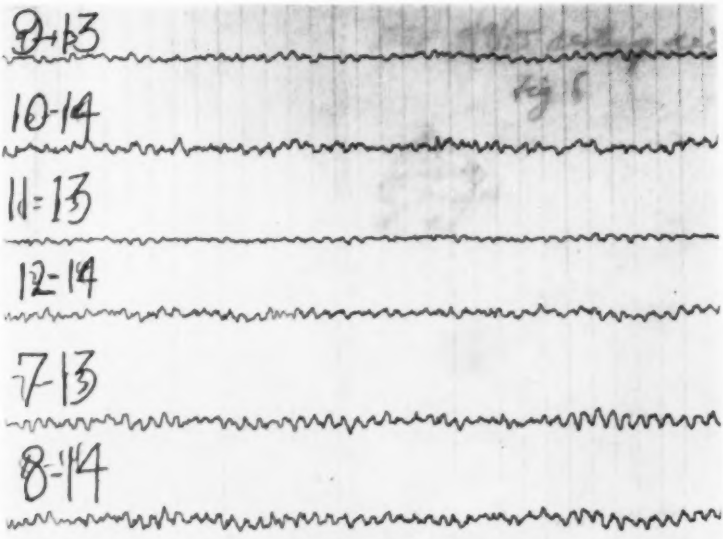
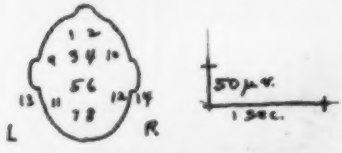


FIG. 6. E.G. RESTING RECORD



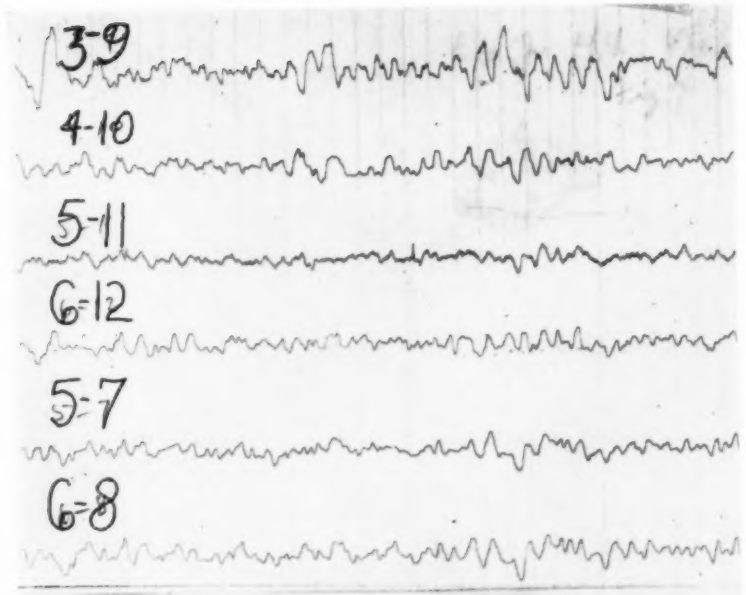
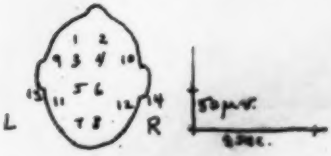


FIG. 7 E.G., JR. HYPERVENTILATION RECORD



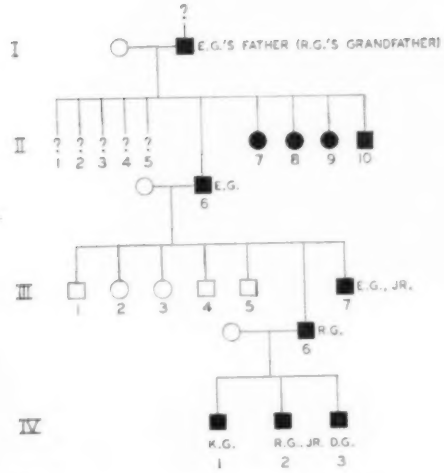


Fig. 8.—Pedigree chart. Prepared according to "The Collection of Records in the Study of Human Heredity" from the Dight Institute of the University of Minnesota, Bulletin No. 2, 1945.

influence. The history of four generations (Fig. 8) of abnormal behavior in this family appears more than just coincidence, although this is a possibility.

As to psychomotor epilepsy, it appears possible from this family study that the episodes may occur at intervals of years and persist for months.

The relationships between abnormal behavior and abnormal brain function of this kind can be clarified only by more electroencephalographic studies on patients who manifest behavior abnormalities, whether hospitalization is required or not.

Mr. Stephen Abramson assisted in the preparation of the electroencephalograms in this study. Dr. Robert Mullin stimulated and arranged for the cooperation of the family in this case.

Room 1808, 1 Hanson Pl. (17).

Effects of Reserpine and Iproniazid (Marsilid) on Space Localization

DONALD M. KRUS, Ph.D.; SEYMOUR WAPNER, Ph.D., and HARRY FREEMAN, M.D., Worcester, Mass.

This study is one outgrowth of a program of research devoted to an analysis of perception from an organismic point of view. This view, the sensory-tonic field theory,[3] has interpreted perception as a function of "organismic-state: stimulus-object" relationships and, accordingly, has systematically integrated facts which show the effects of changes in organismic state on perception. Though a wide variety of conditions affecting organismic state and a number of dimensions of perception have been investigated, of particular pertinence to the present study are the two experiments which follow.

These experiments were based on the assumption that some changes in organismic state possess vectoral qualities which may be expected to have bearing on space perception. For example, the experiences of success and failure seem to be related to "upwardness" and "downwardness," respectively, and one could reasonably expect that the organismic correlates of these experiences would be reflected in changes in perception of the up-down dimension of space. To test this hypothesis, Wapner, Werner, and Krus[4] induced feelings of success and failure in a group of subjects and found that success shifted the apparent horizon—that position in space experienced as being at eye level—in an upward direction, while failure shifted the apparent horizon downward. Greater generality was given to these findings by Rosenblatt,[2] who found that the apparent horizon was located significantly higher in a group of patients diagnosed as being in the manic phase of manic-depressive psychosis than a group of patients diagnosed as being in the depressed phase; a normal group fell between these extremes. The results of these two studies lend support to the general notion that variations in affective state, whether induced by transitory psychological experiences or representing rather permanent characteristics of individual subjects, affect localization in space.

The present study attempts further to extend these findings by studying the effect of pharmacologically induced changes of organismic state on space localization.

It appeared plausible to assume that the so-called energizing and tranquilizing drugs were pharmacological means of inducing changes in organismic state susceptible to characterization in terms of up-down vectors. On the basis of this assumption, it was hypothesized that the location of the apparent horizon would shift in an upward direction for energizers and downward for transquilizers. A limited pilot study * with a single normal subject provided some encouraging results and led to the present systematic study of the hypothesized effects of the energizer iproniazid (Marsilid) and the tranquilizer reserpine, on the position of the apparent horizon.

Submitted for publication June 16, 1958.

Marsilid (iproniazid) was supplied by Hoffmann-LaRoche, Inc., Nutley, N. J.

Drs. Krus and Wapner are located at the Department of Psychology and the Institute of Human Development, Clark University; Dr. Freeman, at Worcester State Hospital.

This investigation was supported in part by a grant, MY 2262, from the National Institute of Mental Health of the National Institutes of Health, U. S. Public Health Service, and in part by the Dementia Praecox Project, Worcester State Hospital.

* Pilot studies were conducted in collaboration with Dr. C. C. Bennett, Boston University.

Apparatus and Procedure

The S, seated in a dark room, was presented with a luminous square measuring 20 by 20 cm. Horizontally bisecting the square was a black line, which the S was instructed to fixate; S's task was to instruct E how to move the figure so that the black line appeared at eye level. S was seated 2 meters from the stimulus figure, and his head was fixed by an adjustable headrest and chin-rest to eliminate head and trunk movements.

The luminous square was so mounted on a rack-and-gear device that it could be moved in small steps up and down along a plumb line directly in front of S. The objective horizon was ascertained separately for each S; this was achieved by measuring the height of S's pupils above the floor. The black line horizontally bisecting the stimulus figure was always placed initially at the objective horizon.

Each S carried out the task of locating his apparent horizon under three conditions: Condition A, two to three hours following oral administration of 2 mg. of reserpine; Condition B, two to three hours following oral administration of 100 mg. of iproniazid, and Condition C, two to three hours following oral administration of a placebo. Twelve S's were tested under each of the three experimental conditions. Sequence was controlled by the use of a 3×3 Latin-square design: four S's were tested in the sequence ABC, four in sequence BCA and four in the sequence CAB. One week was interpolated between experimental conditions, and the study was carried out using a double-blind technique.

Two trials were given in each condition, and the measure employed in the analysis was the mean for the two trials.

The S's consisted of chronic male schizophrenics at Worcester State Hospital. The ages ranged from 32 to 58, with a mean of 49, whereas duration of hospitalization ranged from 5 to 45 years, with a mean of 18 years.

Results

The results are summarized in the Table, which gives the *F*-tests along with the mean positions of the apparent horizon for each of the experimental conditions. Consonant with the hypothesis, the mean position of the apparent horizon is significantly lower under reserpine (mean = −3.2 cm.) than either *without* any drug (mean = +1.1 cm.) or *with* iproniazid (mean = +1.6 cm.). Though in the expected direction, the mean position of the apparent horizon under iproniazid does not differ significantly from that under control conditions.

Effect of Reserpine and Iproniazid on Apparent Horizon

Source	*df*	*MS*	*F*-Tests *F*	*P*
All subjects	11	349.97	--	--
Sequence	2	658.58	2.34	>0.05
Ind/seq.	9	281.17	--	--
Conditions	2	81.75	3.77	<0.05
Order	2	100.34	4.63	<0.05
Sq. uniq.	2	0.58	<1.00	
Error residual	18	21.67	--	
Total	35	131.59	--	

Means *
Reserpine = −3.2 cm.
Iproniazid = +1.6 cm.
Placebo = +1.1 cm.

* A plus score indicates a position above the objective horizon; a minus score indicates a position below.

Comment

The results with reserpine are in keeping with the hypothesis insofar as this drug, a tranquilizer, shifts the apparent horizon downward. Contrary to expectation, however, no significant change in position of the apparent horizon was found with iproniazid. The discrepancy in these results can perhaps be understood in the light of earlier work on the relationship between affective state and apparent horizon. It will be recalled that the two studies cited earlier in this paper[2,4] provide evidence that under feelings of elation and success the apparent horizon shifts upward, and under feelings of depression and failure the apparent horizon shifts downward.

It may be that a necessary condition for drug-induced shifts in apparent horizon is a change in affective state, i. e., any physiological changes due to drug must be accompanied by changes in affect for perceptual change to occur.

This interpretation is supported by the behavioral reports found in the literature for the two drugs used in this study. Reserpine, which produced the systematic change in the apparent horizon, is accompanied generally in greater degree than other transquilizers by feelings of depression. In contrast, iproniazid, which produced no significant change in apparent

horizon, is neither consistently nor with high frequency accompanied by feelings of elation. Crane,[1] for example, reports virtually equal frequency of elation, euphoria, and depression in patients undergoing iproniazid therapy. Moreover, it may be that iproniazid results in changes in affect only if it is administered to initially depressed people, that is, if it results in a change from depression to a normal level of affect. Still another possibility is that cumulative dosages of iproniazid are required before mood changes and accompanying perceptual changes will occur.

This interpertation suggests a definitive hypothesis which requires test, namely, that significant shifts in the apparent horizon occur under drugs only insofar as they have concomitant affective components; e. g., these shifts are upward for energizers of this nature and downward for such tranquilizers. It would therefore be appropriate to design an experiment in which the position of the apparent horizon is measured under the influence of energizers and tranquilizers, representatives of each of which do and do not have affective concomitants. In such an experiment it would be necessary to obtain subjective reports concerning mood, which then could be correlated with positions of the apparent horizon.

If the preceding hypothesis is substantiated, it, on the one hand, has implications for a general theory of perception and, on the other, would offer a sensitive objective measure for differentiating affective changes under various psychopharmacological agents. In terms of a general theory of perception, the present study, however limited, adds to the body of evidence that variations of affect—depression versus elation—evoke organismic changes in terms of up-down vectors which are reflected in corresponding perceptual changes. In one study these variations represented relatively permanent characteristics of abnormal subjects; in a second study such variations were transitory in that they were laboratory-induced experiences of success and failure, and in the present study the variations were also transitory but were induced by pharmacological means.

Summary

This study is concerned with the effect of drugs on the perception of space. More specifically, it is concerned with the effect of a tranquilizer, reserpine, and an energizer, iproniazid (Marsilid), on the apparent horizon—that position in space experienced as being at eye level.

It was found that, compared with control conditions (placebo), the position of the apparent horizon shifted significantly downward under the influence of reserpine and shifted upward, though not significantly, under iproniazid.

The implications of these results are discussed in terms of general perceptual theory, as well as in terms of their significance for differentiating various psychopharmacological agents.

Dept. of Psychology, Clark University.

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Evaluation of the Sedation Threshold Test

DONALD BOUDREAU, M.D., New York

During the past few years a number of articles have been published by Shagass and others [1-5] describing an objective means of evaluating clinical psychiatric data. This is known as the sedation threshold and is determined clinically after intravenous injection of amobarbital (Amytal) sodium by slurring of speech and, more precisely, by the EEG changes produced by barbiturates. By means of this method, there were obtained a number of interesting findings which seemed to warrant further investigation. The purpose of the present study was (1) to test the reliability of the technique and to determine how accurately it could be reproduced; (2) to examine the correlation of the sedation threshold with certain diagnostic categories and with manifest anxiety, and (3) to evaluate the stability of the threshold in nonpatient controls or in patients whose psychopathology remained constant.

Method

The method of determining the threshold corresponded to that originally described except for several minor variations. Briefly, the technique, as outlined by Shagass, consisted of the intravenous injection of amobarbital sodium at a specified rate, resulting in slurring of speech and in the marked increase of fast frequency activity (15-30 cps) on the electroencephalographic tracing. The amplitude of the 15-30-cps activity was measured and a dose response curve plotted. The curve was said to be S-shaped and to contain an inflection point preceding which the amplitude rises sharply and following which the curve tends to form a plateau (Fig. 1). This was not found to be characteristic, however, in that more than one inflection point was frequently found, as shown in Figure 2. The sedation threshold was defined as the amount of amobarbital sodium, in milligrams per kilogram of body weight, which is required to produce the inflection point in the amplitude curve of frontal fast activity. Anxiety and other psychopathological factors were evaluated by two psychiatrists prior to the onset of testing.

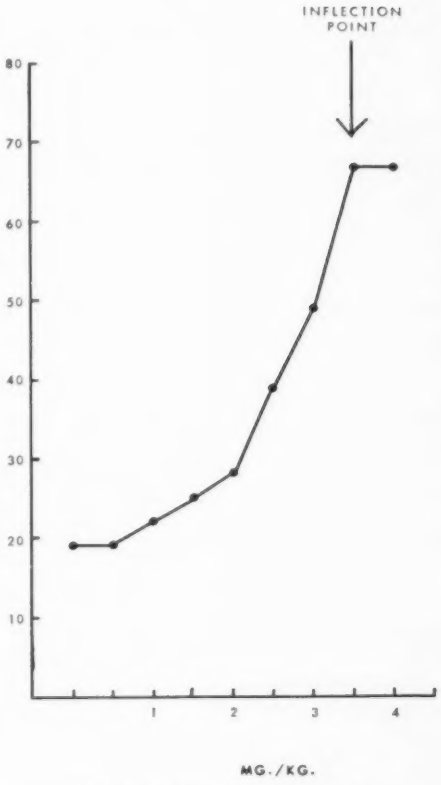

Fig. 1.—Typical S-shaped curve.

The technique used in the present study varied slightly in that slurring of speech was not used as a clinical guide to the threshold, since our experience was similar to that of Thorpe and Barker,[6] who found that this method lacked objectivity, and was therefore of little use in the determination of the inflection point. Second, an Offner frequency analyzer was used throughout the study in an effort to make amplitude measurements of the entire bi-

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From the Department of Psychiatry, New York Hospital-Cornell Medical Center.

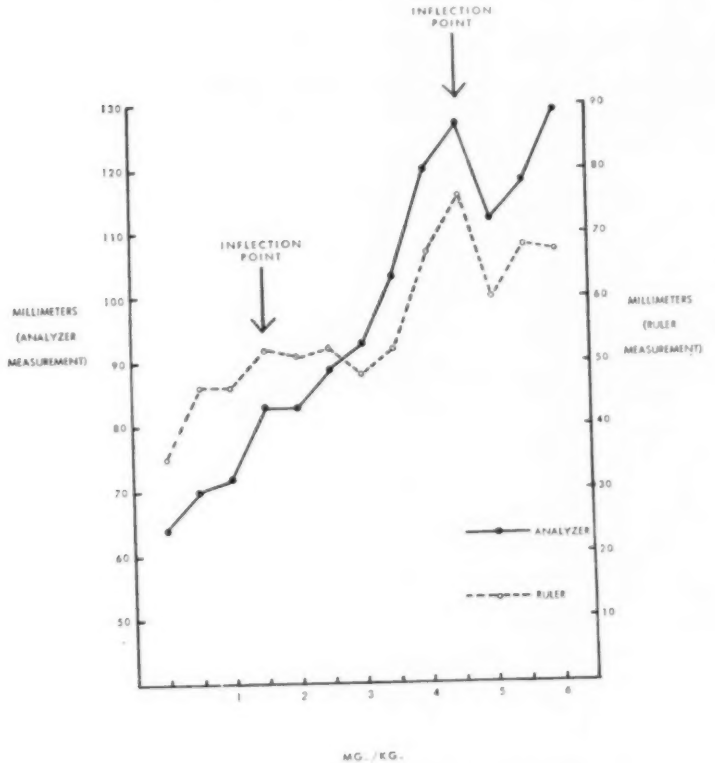

Fig. 2.—Curves showing equivocal inflection points.

frontal tracing during the period of injection. Often, this was not possible because of the intervention in the tracings of muscle artifact. In such cases, only the EEG tracing which was free of muscle activity was measured. In a number of cases hand-ruler measurements were also made.

To test the stability of the sedation threshold, four tests were performed at weekly intervals on a patient whose psychopathology remained unchanged during this period. In addition, two nonpatient controls were each tested four times at weekly intervals.

Subjects

Patients were selected from the inpatient service of the Payne Whitney Psychiatric Clinic. They were chosen for the degree of manifest anxiety they demonstrated and the diagnostic category into which they fell. A total of 60 tests were performed on 36 patients and 3 controls. Of the patient group, 25 were female and 11 male, the ages ranging from 18 to 72 years. The three nonpatient controls were nurses who exhibited no psychopathology, either clinically or as detected by MMPI testing prior to sedation-threshold determination.

Results

Of the 60 records obtained, 19 had to be rejected primarily because muscle artifact interfered in their accurate measurement. Other reasons for rejecting the tracings were the faulty operation of the analyzer and a mild reaction in a patient following administration of amobarbital sodium. Another nine records, although measurable, showed no characteristic S-shaped curve, and consequently no inflection point could be determined. There remained, therefore, a total of 32 records which produced sedation threshold values. Of these, eight were nonpatient controls. In an analysis of the 24 valid records obtained on patients, there was

Correlation of Sedation Threshold with Psychiatric Diagnosis

Mean Sedation Threshold	No. of Tests	Diagnosis	Sedation Threshold: 3.5 Mg/Kg. or Less	Sedation Threshold: 4.0 Mg/Kg. or More
2.50	1	Hysterical depression	100%	0
2.80	5	Character disorder	80%	20%
2.81	8	Psychotic depression	75%	25%
3.00	4	Chronic schizophrenia without deterioration	75%	25%
5.40	5	Neurotic depression	0	100%
7.50	1	Mixed neurosis	0	100%
2.75	8	Nonpatient control	75%	25%

found to be no correlation between the sedation threshold and the degree of manifest anxiety as clinically evaluated by two psychiatrists. In regard to diagnostic categories, however, our results were roughly comparable to those obtained by Shagass (Table). Thus, the sedation thresholds of hysterical and psychotic depressions were grouped at the lower end of the scale (mean sedation threshold 2.50 and 2.81 mg/kg., respectively), while neurotic depressions and mixed neuroses were at the upper end (5.40 and 7.50 mg/kg., respectively). Chronic schizophrenic illnesses without deterioration occupied a midpoint on this scale. The two columns on the right-hand side of the Table indicate the percentage of cases either above or below the arbitrary dividing line of 3.5-4.0 mg/kg. The results of our evaluation of the stability of the sedation threshold method are shown in Figure 3. In the first nonpatient control the sedation threshold varied from 2.0 to 4.5 mg/kg., it being different on each successive week. In the second control subject the threshold varied from 1.5 to 3.5 mg/kg., the threshold being the same on two successive weeks. Similarly, in a patient whose psychopathology, primarily anxiety and depression, did not vary over a four-week period, the sedation threshold fluctuated from 2 to 3 mg/kg. and was the same on two successive weeks.

Comment

As already indicated, the technical difficulties inherent in the determination of the sedation threshold are considerable. Records from 28 tests had to be rejected, either because muscle activity interfered with the

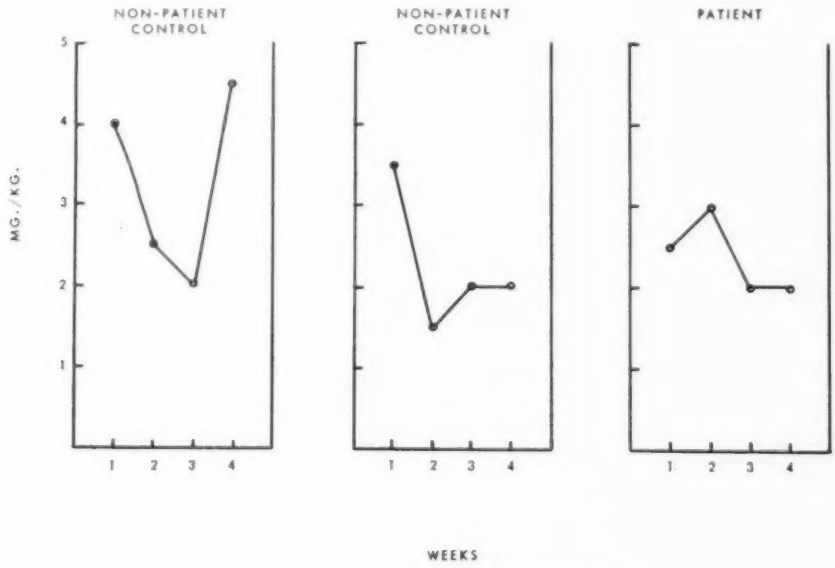

Fig. 3.—Sedation thresholds on successive weeks.

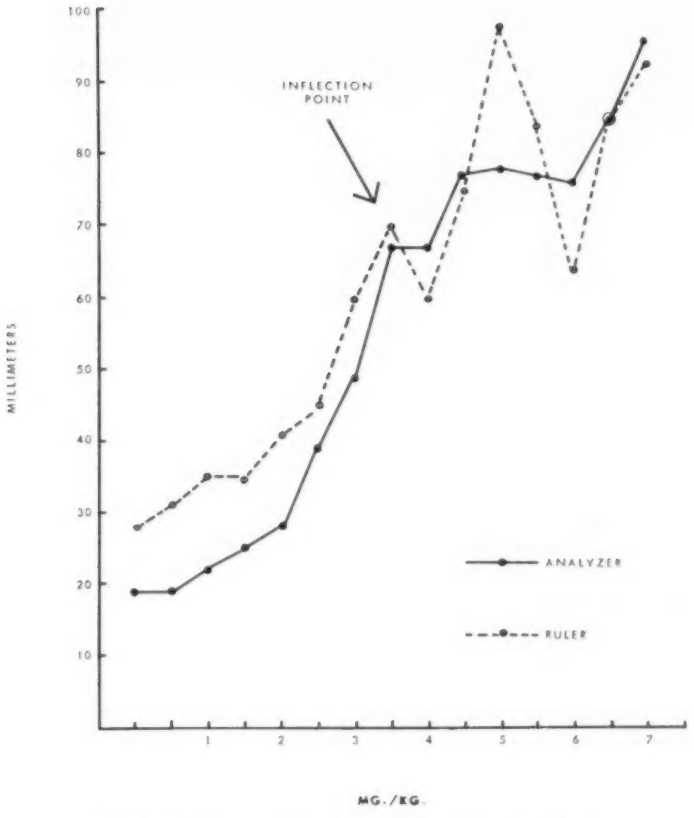

Fig. 4.—Curves showing easily determined inflection points.

accurate measurement of the record or because no inflection point could be determined on the amplitude curve. In Figure 4 the inflection point, obtained from ruler and analyzer measurements of one of the EEG tracings in this series, is definite. In other cases, there were several inflection points, and there was doubt as to which one should be considered indicative of the threshold (Fig. 2). In the present series, it was found that in one-half of all the curves, the inflection point was equivocal. These findings illustrate the difficulties in determining a valid sedation threshold by the method originally described by Shagass.

The problem of fitting various psychiatric entities into definite diagnostic categories is difficult and subject to individual variations, depending to some extent upon the views of the diagnostician. The diagnostic groupings of Shagass do not correspond to a recognized psychiatric classification. Since the primary difficulty occurs in distinguishing psychotic and neurotic depressions, it would seem necessary to classify the cases used in this study according to a standard nomenclature. The psychotic depressions in the Table, tabulated in terms of the A. P. A. classification,[7] are as follows: involutional psychotic reactions, 2; manic-depressive reaction, depressed type, 2; psychotic depressive reactions, 4. Of the neurotic depressions in the Table, only two cases fall into the depressive reaction type of the A. P. A. classification. One case was a postpartum depression, and the other case, tested on two

occasions, was similar to the neurotic depression type as described by Shagass. As regards the diagnoses of hysterical depression and mixed neurosis in the Table, the former concerned a 39-year-old woman whose illness started with a psycholeptic attack and who experienced persistent depersonalization during the period of observation. The case of mixed neurosis was that of a 20-year-old girl who prior to hospitalization had a period of amnesia but who in general showed compulsive traits.

Thus, although Shagass' results in regard to diagnostic categories are striking, and are supported by the findings in this study, there is need for more detailed description of the psychopathology involved.

The lack of correlation between clinical ratings of anxiety and sedation threshold values must be due in part to the difficulty in obtaining an accurate clinical evaluation of anxiety and its psychopathological significance.

The failure of the threshold to remain constant in a patient or in controls in whom there was no observable change in psychopathology will require further study. The results of this series of tests would suggest that the threshold is not a stable biological characteristic of the individual patient.

Conclusion

Because of various technical difficulties, the sedation threshold is difficult to determine and often equivocal. In this series of cases, there was a definite correlation between sedation threshold and various diagnostic categories, particularly as applied to Shagass' concept of psychotic and neurotic depression. Yet no correlation existed between manifest anxiety and the threshold. In addition, the sedation threshold was not found to be a stable value in control subjects or in a patient whose psychopathology did not change clinically.

Payne Whitney Psychiatric Clinic, 525 E. 68th St. (21).

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Suicide and the Medical Community

JEROME A. MOTTO, M.D., and CLARA GREENE, R.N., San Francisco

Doctors have been reminded of their role in the prevention of suicide for decades. They have been advised, admonished, instructed, and exhorted to recognize the signs and symptoms of depression and to appreciate the impressive implications of statistics showing suicide to be a major cause of death. And the suicide rate has shown a steady over-all decline. The year 1956 saw a record low in the United States of 9.7 suicides per 100,000 population,[1] as compared with 11.2 per 100,000 in 1945 and 15.6 in 1930, and 1957 figures promise a continued decline. Is this trend the fruit of a preventive effort by the medical community? Are doctors responding by recognizing potentially suicidal persons earlier than before, and taking steps to forestall suicide? Or does the role of the doctor continue unchanged, while increasing provision for economic and social security, as well as ever greater comforts in everyday living, joins to push the suicide rate down?

In order to answer these questions, one must first ask: "How much contact had there been between the group of persons who committed suicide, those who unsuccessfully attempted it, and the medical resources of the community in which these acts occurred? What chance did these persons offer a physician to take preventive action?" In order to find such information, and from it to estimate the physician's present role in the problem of suicide, we undertook this investigation. San Francisco, a prominent center of medical training, research, and practice, and a metropolitan area with a suicide rate (29.4) three times that of the nation and twice that of the State of California,[1] provided an appropriate setting for the study.

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Instructor in Psychiatry, University of California School of Medicine (Dr. Motto). Instructor in Nursing, San Francisco City and County Hospital (Miss Greene).

Material and Method

The data are taken from 175 successive cases of suicide in San Francisco from November, 1956, to September, 1957, and the 197 admissions to the San Francisco City and County Hospital for suicide attempts during the same period—a total of 372 cases. Information was obtained from the patients themselves when possible, and from relatives, police, hospital charts, and coroner's reports. Emphasis was placed on the following questions:

1. Was the patient in touch with a doctor within the six-month period preceding the suicide or the suicidal attempt?
2. What was the doctor's specialty, if any?
3. What were the patient's complaints?
4. What was the duration of medical care?
5. How long before the suicidal act did he last have medical contact?
6. How often was the medium of medical treatment used as the means of self-destruction?

In a sizable group, detailed information could not be obtained. Some patients refused to give the requested information or gave vague or conflicting replies. Some were discharged from the hospital before they could be interviewed, or were transferred to another facility before they had recovered sufficiently to talk. Often the coroner's report either did not refer to prior medical care or indicated recent medical care without specific details.

Since unsuccessful suicide attempts often reflect greater differences in desire for death than successful suicides do, the former were graded in Classes I to IV to specify the seriousness of the act. Class IV contains those who would have died but for a quirk of fate or heroic medical effort; e.g., a woman who leaped from the roof of a five-story building survived despite the shock and multiple fractures. Those whose suicidal acts were judged a "gesture" were put in Class I, e.g., a sociopath who in jail superficially cut his wrists with broken glass "to convince them I should be in a hospital." Class II includes those who quickly called for help or took nonlethal amounts of a familiar drug. When potentially fatal steps were

taken in a setting where the person apparently knew he would soon be found, he was placed in Class III.

Findings *

For the suicide group, in 74 (42%) of the cases the patient had had some known medical contact during the six months preceding the act; in an additional 17 (10%) there was probable contact; for example, relatives stated that one patient "feared return to the hospital," without giving further details. Only 4 patients (2%) were known to have had no medical care during that period. In 80 (46%) there was insufficient information, but the fact that 47 (27%) in this group committed suicide with a barbiturate suggests that some medical contact had taken place.

For the unsuccessful suicide attempts the data are even more striking, in that 116 patients (59%) had been in touch with a physician and 52 (27%) had not; in 27 cases (14%) insufficient information was obtained (Table 1).

The 227 physicians involved in the reports of all 372 cases represent every major medical specialty except pediatrics. When the patient was seeing more than one doctor at the same time, each was listed; however, if one was a psychiatrist, his was counted as the specialty. If the patient was seen in a clinic, the specialty of the clinic was counted. Numerically, psychiatrists lead the list; 15 (9%) of the patients who committed suicide had seen a psychiatrist within the prior six months, and 29 (15%) of those making an unsuccessful attempt had done so. General practitioners, a close second, were consulted by 9 (5%) of the persons who committed suicide and by 31 (10%) of those who failed in a suicide attempt. Internists come next, having previously seen 9 (5%) suicides and 13 (7%) attempts. Hospital staffs, both public and private, saw 15 (9%) suicides and 11 (6%) attempts prior to the act, and in a total of 60 cases (16%) the specialty could not be determined. The distribution of cases among the various specialties is summarized in Table 2.

Since medical contact is often sporadic and of varying type, statements regarding the duration of such contact can be quite misleading. Two interviews of an hour each on successive days may provide a sounder basis for judgment regarding suicidal risk than years of intermittent brief visits for management of a chronic or recurrent illness. Twenty-two (13%) of those who committed suicide and 62 (31%) of those who attempted to do so had been in touch with a physician for a month or longer before the act. Five (3%) of the suicides had seen the doctor only once—8 (5%) for up to a 30-day period and 50 (29%) for an undetermined time. Of those making unsuccessful attempts, 19 (10%) had only one visit, 38 (20%) up to 30 days' contact, and

* All percentages are relative to the *total sample* of suicides or unsuccessful suicide attempts unless specified otherwise.

TABLE 1.—*Suicide and the Medical Community*

Total Sample	Suicides 175	Attempts 197
In touch with physician within 6 mo.		
Yes	74 (42%)	116 (59%)
No	4 (2%)	52 (26%)
Probable	17 (10%)	2 (1%)
No information	80 (46%)	27 (14%)

TABLE 2.—*Distribution of Specialties Among Physicians Attending Suicidal Patients*

Total Sample	Suicides 175	Attempts 197
Specialties		
Psychiatry	15	29
General practice	9	31
Internal medicine	9	13
Obstetrics and gynecology	0	9
City physician	4	5
Surgery	1	4
Neurology	0	2
Urology	0	2
Ophthalmology	0	2
Chest diseases	1	1
Orthopedics	1	1
Dermatology	0	1
Endocrinology	0	1
Public hospital	11	5
Private hospital	4	6
Undetermined	25	35

TABLE 3.—*Suicide and the Duration of Medical Contact*

	Suicides	Attempts
Total Sample	175	197
Duration of contact		
One visit only	5 (3%)	19 (10%)
1-30 days	8 (5%)	38 (19%)
Over 30 days	22 (13%)	62 (31%)
Undetermined	50 (30%)	19 (10%)
No information	90 (49%)	59 (30%)
Time from last contact to suicide attempt		
Same day as attempt	6 (3%)	8 (4%)
1-7 days	11 (6%)	34 (17%)
8-30 days	12 (7%)	36 (18%)
31-180 days	13 (7%)	25 (13%)
Undetermined	51 (29%)	10 (5%)
No information	82 (48%)	84 (43%)

19 (10%) an undetermined period of care (Table 3).

The question of elapsed time between the last visit to the doctor and the suicidal act is a crucial one in formulating a preventive approach. It is most unfortunate when a patient leaves a doctor's office and kills himself later the same day. This is what happened in six (3.5%) of the cases studied. Eight (4%) more patients made unsuccessful suicide attempts on the same day as their last visit, and the 61 (51 suicides, 10 attempts) for whom details were not available might well furnish additional cases. Eleven patients (6%) were seen within a week before their suicide, as were 34 (17%) who attempted it, and similar numbers of cases were seen in the time intervals of one week to one month and of one to six months before their suicidal act (Table 3).

To add salt to the physician's wound, 53 patients (14%) used the medication prescribed for the suicidal weapon (12 suicides, 41 attempts). The fact that 81 (22%) (47 suicides and 34 attempts) of the persons for whom no medical contact could be determined attempted suicide with a drug that can be obtained only by a medical prescription suggests that other efforts at therapy were similarly misused (Table 4).

The complaints these patients brought to the physician covered a wide range, but most frequently involved manifestations of depression, a symptom pointed out in numerous prior studies.[2,3,9] A feeling of depression was the commonest complaint recorded for the suicide group, followed, in order, by abdominal distress, nervousness, the routine of surgical follow-up after operation, and apprehension. The patients who made unsuccessful suicide attempts put nervousness at the head of the list, followed by depression, insomnia, headache, abdominal distress, anorexia, black-outs (epilepsy), and pregnancy.

The old dictum that a history of prior suicide attempts is a valuable indicator of current possibilities finds support in this group of cases. Of the 22 suicides for whom such data were available, all but 1 had a history of at least one earlier attempt. Of the 197 who made unsuccessful attempts, 58 (30%) had such a prior history, and 104 (53%) made the first attempt; the data were insufficient to determine this factor in the remaining 35 (17%).

In discussing unsuccessful suicidal acts, the question invariably arises as to the seriousness of the person's intent—whether his goal was primarily to control his environment by this action rather than to do harm to himself. For the purpose of this study it is assumed that every person who successfully committed suicide consciously intended to end his life, though a careful appraisal of each case would probably reveal several exceptions to this. Classification of the unsuccessful suicide attempts according to the criteria described above represents an effort to evaluate the seriousness of the act as a threat to the person's

TABLE 4.—*Suicide and the Source of Drug*

	Suicides	Attempts
Total Sample	175	197
Prescribed medication used as suicide agent	12 (7%)	41 (21%)
Prescription drug used without known source	47 (27%)	34 (17%)
Classification		
I		33 (17%)
II		76 (39%)
III		50 (25%)
IV		38 (19%)

life. Thirty-three (17%) fall in Class I (least serious), 76 (39%) in Class II, 50 (25%) in Class III, and 38 (19%) in Class IV, which includes those whose attempts indicated every intention of self-destruction.

Comment

It is very difficult to investigate the successful efforts physicians make to prevent suicide; thus, the failures come to the fore. We should like here, however, to shift the emphasis from this investigation of the patient (and the welter of statistics used to describe him) to the physician and the role he fills in shaping the suicide problem. Such a shift may cause doctors some discomfort, but it is an essential step, neglected so far, in increasing the effectiveness of preventive efforts in this field. This is not to underestimate the frequency with which doctors do successfully prevent a suicidal act. We do not know how often this occurs, and this question must also be explored before a clear picture of the suicide problem can be obtained.

Most experienced physicians readily recognize the presence of emotional disturbances, including depression, and are well aware of the importance of suicide as a major cause of death. Yet, as apparent from the data, their patients continue to commit suicide despite current or recent medical attention. Specifically, at least one out of every six persons who committed suicide during the period of the study had been seen by a doctor during the preceding 30 days; nearly one-half had had medical care within the preceding 6 months, and one out of three killed himself with a drug available only on a physician's prescription. The figures for unsuccessful suicide attempts are somewhat higher, with two out of every five having seen a doctor within one month, nearly three out of five receiving medical attention within six months of the attempt, and two out of five using a prescription drug to attempt suicide. The percentages for both groups necessarily understate the factors involved, since a large number of cases providing incomplete details is included, and further information would thus push the figures higher.

Anxiety in the physician regarding suicide, a critical factor in the management of suicidal patients, may help to account for this situation. The presence of such anxiety increases the difficulty of either clearly assessing the patient's emotional state or providing emotional support. Cultural attitudes toward suicide join with professional pride and personal abhorrence to cause the doctor to deny to himself that such a step may be imminent, and hence to avoid taking preventive measures. The intensity of anxiety that may surround this issue is clearly exemplified by one physician who declined to provide the coroner's office with information about a patient who had committed suicide, stating he was unable to do so without the patient's permission!

It is striking that the commonest complaints recorded in the suicide group include despondency and nervousness. These suggest the presence both of emotional illness and potential suicidal risk, either of which may create enough anxiety in the physician to interfere with his thorough exploration of each possibility. The internal pressure to deny the urgency of such factors increases with the prestige of the patient; the embarrassment of asking a prominent person about suicidal impulses often poses a severe hurdle that is never quite overcome. Oliven[4] suggests useful ways of broaching it effectively, recognizing the doctor's anxiety as a block to his carrying out a careful evaluation. Schmidt, O'Neal, and Robins[5] found that patients making unsuccessful suicide attempts frequently told the physician of their having depressed feelings, but rarely mentioned their suicidal plans. This omission is ascribed to the physician's failure to ask about such plans, however, rather than to the patient's reticence. One recalls here the adage ascribed to Osler that more things are missed by not looking than by not knowing.

Schmidt and his co-workers further report that of 109 unsuccessful suicide attempts studied, 71% (25) of the "serious" and 49% (36) of the "not serious" attempts had been made by patients under a physician's care at the time, and 45% (49) of all patients had seen their private physician within three months before their admission. Parnell and Skottowe [6] investigated this factor in 100 suicides and found that 27% had "recently" been under a doctor's care (17% had seen a general practitioner and 10% a general practitioner and a "consultant psychiatrist"). These investigators, however, do not define or describe in detail the nature or extent of the medical contact.

Of course, even the most accurate statistical picture may be misleading. The repeated statistical item that the suicide rate among white male physicians is twice that of the white male population [8-10] is quite true. But it is startling only until the physicians' suicide rate is compared with that of the white male population *in the same age group*, when the difference is seen to be not significant.[11,12]

These few reports, which only begin to scrutinize physician-patient contact and suicide, may help, as it is hoped the present paper will do, to point the way to a more searching study of this vital aspect of the suicide problem.

Summary

The degree of contact that suicidal persons have with the medical community prior to making a suicide attempt was investigated in 175 consecutive suicides and 197 unsuccessful suicide attempts in San Francisco from November, 1956, to September, 1957.

1. At least 40% (74) of the suicides and 60% (116) of the attempted suicides were under medical care, or had been so within the prior six months.

2. All major medical specialties were involved except pediatrics; psychiatry, general practice, and internal medicine accounted for nearly half (47%) of the 227 physicians known to have treated these patients.

3. Patients complained most frequently of nervousness, depression, insomnia, abdominal distress, headache, apprehension, and seizures. Routine postoperative follow-up and pre- and postpartum care also demanded attention as situations preceding a suicide attempt.

4. Of the entire group, 84 (23%) had been in touch with a physician for at least a month before the act. In 59 (16%) instances the suicidal act occurred within a week of the last medical contact, and in 14 (4%), on the same day the doctor was seen. Another 147 (40%) of the patients had seen a doctor within six months of the suicidal act.

The medical community is seen to be extensively involved in the suicide problem.

The degree and kind of contact between members of the medical community and suicidal persons, especially the physician's anxieties about suicide, are suggested as factors that should be studied further in assessing the physician's role in suicide prevention.

Dept. of Psychiatry, University of California School of Medicine.

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Mechanism of Denial in Physical Disabilities

SAUL H. FISHER, M.D., New York

Since the first description of denial of blindness by von Monakow, in 1885, and the introduction of the term *anosognosia* by Babinski, in 1914, to denote denial of left hemiplegia, this phenomenon has attracted the attention of many authors. The vast majority of the reports have been concerned with brain-damaged patients; and, although there have been instances of denial of physical disability without brain damage, such as paraplegia and amputation, most authors have been concerned with the former.

Because of the emphasis on brain damage, a number of theories have arisen to localize the kind of damage which predisposes to denial of illness. The recent monograph of Weinstein and Kahn[1] has questioned this approach and has pointed out that, given something to be denied, not only disordered brain function but the milieu, time, and premorbid personality are also determining factors. While Weinstein and Kahn based their studies entirely on brain-damaged patients, they emphasize that denial "is not peculiar to patients with brain disease, but has much in common with symbolic modes of expression used under normal conditions of brain function." They refer to dreaming and sleep, and the behavior of children.

Actually, denial has a much broader meaning than is ascribed to it by emphasis on brain damage. It does occur in physical disabilities without brain damage, and it can manifest itself in a variety of degrees and manners. It is the purpose of this paper to emphasize these points by means of three case presentations.

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Assistant Professor of Clinical Psychiatry, New York University College of Medicine, and Director of Psychiatric Services Division, Institute of Physical Medicine and Rehabilitation, New York Hospital-Bellevue Medical Center.

Report of Cases

CASE 1.—A 34-year-old white woman had suffered a broken back at the age of 16, after being thrown from a horse. Following a period of hospitalization and treatment, she was left with spastic paraparesis. Actively seeking and obtaining rehabilitation, she finally reached the point where she walked with a scissors gait and with the assistance of a cane. Her life from then on seemed quite normal and rather full and interesting. She married a young writer, and, unable to have children of her own, she proceeded to adopt three. She moved to the suburbs, cared for her home and family, was a prime force in starting a nursery school, wrote several children's books, was active socially, and was highly regarded in her community.

One summer she and her family spent a week vacationing with friends in a neighboring state, in the course of which the friends took movies of everyone. The patient did not see the movies until the following summer, when the vacation trip was repeated. At this time her host projected the films of the previous summer, and, among the various sequences, there was one of the patient which revealed her walking down a path. The patient was shocked by what she saw. While she had never denied the fact of her disability, she had always thought that she walked more smoothly than she actually did. The films startled her. She saw herself as ungainly, awkward, crippled, and ugly. She experienced profound depression, and after her return home was unable to function. She withdrew from community activities and social life. She was preoccupied with feelings of ugliness and of failure, and it was at this time that she presented herself for treatment.

The patient was not unknown to me, for her husband had been a patient previously. While her husband had a good deal of respect for her, he saw her as a demanding and controlling person, who attempted to run her home like a military establishment. Both she and her husband were writers, and there was obvious competition between them, which had led to work blocks in him. There

had been several conferences with the family, so that a predepression estimate of her was available. While it was true that she did have a need to dominate and control, some of it had been provoked by immature and uncooperative attitudes on the part of the husband. He would refuse to help her with certain chores which were realistically difficult for her. The impression at that time was that, whatever her problems, she seemed the more mature and realistic of the two. It was also clear that she had a tremendous drive, which undoubtedly was of a compensating and reparative nature.

Realistically, she had been doing very well indeed, but her image of herself had obviously been distorted. The movies served to break through this image, with the resulting depression.

Treatment was entirely psychotherapeutic, and, although she responded satisfactorily, was prematurely terminated by a decision to move to a warmer and easier climate.

CASE 2.—A 41-year-old white woman of Dutch-Jewish background was admitted to the Bellevue Hospital rehabilitation service with a left-sided hemiplegia. It had been noted in evaluation conference before admission that she was overly cheerful, optimistic, confident, and somewhat euphoric. She was in a wheel chair and unable to walk, and the rehabilitation goals were directed toward ambulation. After her first visit to the ambulation room, the patient became very depressed, wept, shouted, threatened suicide, was abusive to other patients and the staff, was sexually seductive, and would shock the staff with florid descriptions of her sexual prowess and attractiveness.

The ambulation room of a rehabilitation center contains parallel bars, ramps, and steps, simulating situations such as street curbs, bus steps, etc. In addition, there are full-length mirrors to facilitate the learning process. The patient had viewed herself in the full-length mirror, and it was after this experience that she became depressed and agitated.

The patient's history is an interesting one. She had been an instructor of physical education in her native Holland, but was forced to escape after the invasion by the Nazis in 1940. She made her way to Indonesia, where she continued in her profession. However, the Japanese occupied Indonesia, and she was placed in a concentration camp until the end of the war, suffering both physical and moral privation. After the liberation, she emigrated to this country, where she obtained a position as secretary and assistant to a physician, in which she did exceedingly well and was very well thought of. While here, she met and married a fellow-countryman and had one child. She experienced an acute attack of appendicitis, was operated on, and, after an uneventful recovery, was discharged home. Twenty-four hours later, she suffered a bout of headache, dizziness, and unconsciousness, and was returned to the hospital, where a diagnosis of carotid artery thrombosis with left-sided hemiplegia was established. It was after this episode that she was admitted to the rehabilitation service.

On examination following the mirror episode the patient was in an obvious depression. She spoke of her ugliness and crippled state and expressed feelings of futility regarding her future. She moaned pitifully: "After all I've gone through, why did this have to happen to me?" In addition to this, the meaning of an intact body to this woman, especially considering her occupation as a physical education instructor, became apparent. Her rage against cruel fate, projected onto the doctors and staff, and the compensatory function of her sexual preoccupation were also apparent. All of this was discussed with the staff at conference, and an all-out effort was made to provide her with support, acceptance, and affection. A beautician was called in to do her hair, and, along with rather superficial psychotherapy, she responded and proceeded to participate in the rehabilitation program successfully. She left the hospital, able to ambulate with the assistance of braces and crutches, and returned to her home.

CASE 3.—A 32-year-old white woman suffered an attack of poliomyelitis at the age of 1½ years, following which she had numerous orthopedic corrective operations. Her father deserted the family shortly thereafter, and at the age of 7 she was placed in an institution for disabled children, where she remained until the age of 18. Since then, she has lived with her mother, supported by welfare agencies, and on occasion by an older brother.

When the patient presented herself for psychotherapy, she was paraplegic, walking with crutches and with both legs braced. Her stated reasons for seeking therapy were that (1) she was writing an autobiographical novel, and was blocked on the period of her high school days (the patients at the institution received elementary schooling in the confines of the building but had to attend the local public high school along with nondisabled children); (2) she was fearful of people, was tense and insecure, and felt that people expected so much of her that she would fail them.

Her relationship with her mother was an utterly dependent one. She was unable to dress herself, to get in and out of bed, and to bathe herself, depending on her mother for these skills. On several occasions, social workers associated with the Welfare Department made appointments for her at a rehabilitation center, but on each occasion she would get "sick" and cancel the appointment. On one occasion she visited a psychiatrist, but was unable to continue with him because of intense anxiety and hostility. It turned out that the psychiatrist was also disabled and walked with a severe limp.

The patient was seen three times weekly, and, after four months, feeling secure that the patient was involved and committed to the therapeutic experience, and that a positive transference existed, we urged her to attend the rehabilitation institute, to which she reluctantly agreed. Again, the full-length mirror in the ambulation room was most traumatic. The patient reacted immediately with feelings of inadequacy, ugliness, stupidity, and shame. She was furious with the psychiatrist, as manifested in dreams, in which he was plagued with disorders, such as epilepsy, tuberculosis, and crippling. This reaction was worked through, and the patient stayed with both the Institute and the psychiatrist. At the Institute she gradually came to accept its program, the doctors, and the other patients. She exercised, strengthened her muscles, got new braces and crutches, and within two months was able to get in and out of the bathtub herself and to dress herself. She took courses in shorthand and typing and began to join in the social life of the group. In therapy, basic personality and interpersonal problems were exposed, and her development in these areas, while difficult and painful, was gratifying. After two years, she was physically self-sufficient, had obtained a job in a publishing firm, and had acquired a boy-friend. The only one who suffered from her growth was her mother, who had vigorously opposed both the physical rehabilitation and the psychotherapy, and whose stake in the helplessness of her daughter became quite apparent.

Comment

These cases are not representative of those usually described in the literature. They do not show confabulation, spatial and temporal disorientation, or explicit verbal denial. Two of the three patients had not suffered any brain damage, nor did they reveal any on clinical examination or psychological testing. The patient with carotid artery thrombosis and hemiplegia showed minimal evidence of organic brain damage, but none of the extreme manifestations of the organic brain syndrome.

What is striking about these patients is the manner in which the denial mechanism was ruptured, i. e., via the visual apparatus, and the essential similarity of response to the breakthrough, i. e., depression. All three were concerned with their appearance, which emphasizes the fact that body image is not merely a central spatial representation, but is associated with certain values. All three were concerned with a loss or lack of mastery, on which so much of self-esteem is based.

These cases illustrate, too, that there are varying degrees of denial. Weinstein and Kahn have classified anosognosia as explicit verbal denial, but also have described cases of implicit denial in brain-damaged patients, characterized by withdrawal, inattention, pain asymbolia, alterations in sexual behavior, hallucinations, and mood changes. It is important to note that implicit denial may occur in non-brain-damaged patients as well.

Denial is a basic defense of the individual in the face of a threat to his integrity of person and self-esteem. It is a mechanism employed to distort unacceptable reality and, in so doing, make it possible to exist and to function within that reality. As such, it is a broad-based defense, is seen in physical disability with or without brain damage, and may, as suggested by Ullman,[2] be operative in purely psychological phenomena, such as hypnosis, hysteria, schizoid maneuvers, and dreams, and in sensory deprivation. In each case there is an attempt at repair, and a return to a reality which had been experienced and which provided greater satisfaction and security.

Summary

Three cases of denial of physical disability are presented.

In all three cases denial was broken through via the visual apparatus.

The results in the three cases was depression.

After the breakthrough of denial, all patients responded to psychotherapy and succeeded in their rehabilitation goals.

Institute of Physical Medicine and Rehabilitation, 400 E. 34th St. (16).

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Effectiveness of Dithiazanine Against Worm Infections of Mental Patients

MARTIN D. YOUNG, Sc.D.; GEOFFREY M. JEFFERY, Sc.D.; JOE E. FREED, M.D., and WILLIAM G. MOREHOUSE, M.D., Columbia, S. C.

Recently Frye, Swartzwelder, et. al.[2] (1957) and Swartzwelder, Frye, et al.[1] (1957) reported that dithiazanine, a cyanine dye, was therapeutic against trichuriasis, strongyloidiasis, ascariasis, and enterobiasis (oxyuriasis), and exerted significant activity against hookworm.

Parasitic infections are often severe in mental patients, and the elimination of these infections has proved to be very difficult. The encouraging reports on dithiazanine led to its use here to determine its efficacy against parasitic infections in mental patients.

Materials and Methods

The patients were white women who had been at the hospital for several years. Because of mental deterioration, they were unhygienic in their habits. The average weight was about 54 kg. (120 lb.).

The presence of infections was determined by direct saline and iodine fecal smears and zinc sulfate centrifugal flotation. The intensity of infection was determined by Stoll egg counts. Two stool specimens were obtained from each patient during the week prior to therapy for Stoll egg dilution counts. One and three weeks following drugging, stool specimens were again examined, two each week. The percentage of egg reduction was determined from pre- and post-treatment Stoll egg counts.

The drug was in 100 mg. enteric-coated tablets and was given in 200 mg. doses four times daily for five days. It was given after meals and at bedtime; the latter dose was given with milk or other food.

Results

The results of treatment of 27 patients are summarized in the accompanying Table. Twenty-three of these patients were infected with Trichuris, with densities of eggs per gram ranging from 400 to 276,300. Reduction in egg counts ranged from 83% to 100% one week after treatment and from 54% to 100% three weeks after treatment. One week after treatment 14 patients (61%) showed no eggs and the reduction in total egg count was 96%. Three weeks after treatment 18 patients (76%) were free of eggs and the reduction in total egg count was 99%. Six patients who had been lightly positive the first post-treatment week were negative on the third. Two patients negative on the first post-treatment week

Response of Trichuris and Hookworm Infestations to Dithiazanine *

	Trichuris	Hookworm
Infections treated	23	27
Before treatment		
Eggs per cc.		
Range	400-276,300	500-75,500
Average	26,400	9,600
After treatment, 1 wk.		
Eggs per cc.		
Range	0-17,500	200-17,600
Average	1000	4800
Infections eliminated	14	0
After treatment, 3 wk.		
Eggs per cc.		
Range	0-4900	100-38,400
Average	300	5800
Infections eliminated	18 †	0

* Given in a dose of 200 mg. q. i. d. for five days.

† Only one egg was found after treatment on each of two patients counted as failures.

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Dr. James B. Hammond, Eli Lilly & Company, Indianapolis, supplied the dithiazanine iodide (Delvex) and suggested the dosage used.

Department of Health, Education, and Welfare, U. S. Public Health Service, National Institute of Allergy and Infectious Diseases, Laboratory of Tropical Diseases (Drs. Young and Jeffery). Medical Staff, South Carolina State Hospital (Drs. Freed and Morehouse).

had very few eggs, i. e., 100 and 300 per cubic centimeter, on the third week. As 100 eggs is the smallest number ordinarily detectable by the Stoll dilution count, this finding means that the patients could have been positive also during the first post-treatment week and the occasional egg not found. In other words, the finding of such a few eggs on the third week does not necessarily indicate a return to egg laying after suppression during the first post-treatment period. The results for the aforementioned six patients who were positive the first post-treatment week and negative on the third week support this reasoning.

Worms were often seen in the feces after treatment, but no effort was made to recover all of the worms passed because of the time involved and because this is often impossible with mentally deteriorated patients.

None of the 27 hookworm infections were eliminated, although 7 showed a reduction of approximately 80% by the end of the third post-treatment week. The reduction of total egg count was 50% after one week and 40% after three weeks. In 10 of the patients the egg counts were larger than or remained the same as those prior to treatment at the end of the first week (two patients), or the third week (four patients), or both (four patients).

In 11 patients mild and transient vomiting was reported during the course of treatment; in none of these was it necessary to terminate treatment, nor did the vomiting appear to cause loss of significant amounts of drug. Blue-tinged vomitus was reported from two episodes. Nausea without vomiting was reported by one patient. It is possible that nausea occurred in other patients without being seen by the ward personnel or reported by the patient. Mild diarrhea occurred in two of the patients. The stools were uniformly colored blue. No direct information on blue coloration of urine was available, and in the few instances in which such coloration was reported by the ward attendants there existed the possibility of coloration by fecal contamination of the receptacle.

Comment

These results confirm those of Frye, Swartzwelder, et al.[2] that dithiazanine is a good trichuricide. Further, it appears to be effective against the extremely heavy infections sometimes found in mental patients, a quality which has been difficult to find in other drugs. Also confirmed is the moderate effect of the drug against hookworm reported by Swartzwelder, Frye, et al.[1] Although none of the hookworm infections were eliminated, most of the infections were reduced in intensity.

The larger dosage of drug used by us, namely, 800 mg. per day, seemed to have little added effect on the parasites over the 600 mg. per day used by Frye, Swartzwelder, et al.[2]

Of interest was the occasional increase in hookworm egg counts following treatment. In six cases one week after treatment these increases ranged from 100 to 3600 eggs per gram, and in six cases three weeks after treatment, from 200 to 7400 eggs per gram. This, along with the observation that in hookworm cases the reduction in egg count one week after treatment was somewhat higher than that three weeks after treatment, may indicate that injury to the worm may frequently have produced only temporary suppression of egg production, or may even have stimulated egg production temporarily in some cases. It is quite certain, from the nontreated controls and because of the time of year, that the worm burden did not increase during the treatment period.

Summary

Dithiazanine iodide (Delvex) was tried against hookworm and Trichuris infections in mental patients. Eight hundred milligrams daily in divided doses was given for five days. Of 23 Trichuris infections, 18 were eliminated and the remaining 5 greatly reduced. The over-all egg count was re-

duced by 98.9%. None of the 27 hookworm infections were eliminated. The over-all reduction of hookworm egg counts was 39.6%.

Until the present Trichuris infections in mental patients have been difficult to eradicate. Dithiazanine appears to be very useful in this condition.

National Institute of Allergy & Infectious Diseases, Laboratory of Tropical Diseases, P. O. Box 717.

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An Evaluation of Meprobamate in Opiate Withdrawal

ARNOLD H. ZUCKER, M.D.; STANLEY D. MACHLIN, M.D., and WINFIELD SCOTT, Ph.D., Fort Worth, Texas

Meprobamate has been reported to relieve muscular spasm, insomnia, and anxiety symptoms.[1] Since these findings are prominent in the opiate-withdrawal syndrome, it was hypothesized that meprobamate might be a useful adjunct in the treatment of this illness. To date, only a few isolated observations have been reported. Collomb and Miletto[2] reported that several cases of drug addiction responded favorably. In an evaluation of 65 hospitalized alcoholics and 6 drug addicts, Thimann and Gauthier[3] found that three patients addicted to diacetylmorphine (heroin) showed a "good" response and the other addicts were unaffected.

Meprobamate has been found useful in the treatment of alcoholism by several investigators. Thimann and Gauthier[3] reported that more than 58% of their series showed "marked to moderate" improvement, as manifested by relief of severe anxiety symptoms, subsiding of tremors, and better sleeping and eating. Selling[4] noted that meprobamate helped prevent serious alcohol-withdrawal symptoms. The major symptoms responding were insomnia and tension. In a controlled study of 200 alcoholic patients, Greenberg and co-workers[5] found that meprobamate had a significantly greater effect than placebo in relieving psychomotor agitation, anxiety, irritability, insomnia, and demand for medication in the group of ambulatory, chronic, outpatient alcoholics. In the more acute, hospitalized alcoholics the only symptom that responded significantly was insomnia. It was felt that hospitalization increased the apparent improvement of patients receiving placebo and that extremely disturbed patients responded minimally.

None of these studies deals adequately with the use of meprobamate in the opiate-withdrawal syndrome. To evaluate this, a clinical study was devised at the U. S. Public Health Service Hospital, Fort Worth, Texas.

Experiment

It was hypothesized that meprobamate will favorably modify the opiate-withdrawal syndrome, as determined by standardized observations. The experimental subjects were 62 male patients admitted to the hospital withdrawal ward for treatment of opiate addiction. They ranged in age from 19 to 67 years, the average age being 30. Duration of addiction varied from 1 to 48 months, with an average of 8.4 months. Fifty patients were addicted to diacetylmorphine, five to morphine, and the remaining seven to other opiates. The presence of physical dependency on opiates was determined by withholding all drugs until definite signs of the opiate-withdrawal syndrome were noted. These addicts were then randomly assigned to one of three groups. Excluded from the study were patients who did not manifest clear-cut opiate-withdrawal signs, those using nonopiates, such as barbiturates, alcohol, and tranquilizers, and addicts with significant medical illness.

The study was conducted in the hospital withdrawal ward, in which all newly admitted patients are domiciled. This was a large, closed ward, housing 35 patients in dormitory style. From the nursing station it was possible to observe all the patients directly. The staff was a permanent one which had many years of experience in the treatment of drug addicts. The day shift

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Meprobamate was supplied as Miltown by Wallace Laboratories, Inc., New Brunswick, N. J.

Staff Psychiatrists (Drs. Zucker and Machlin); Clinical Psychologist (Dr. Scott), U. S. Public Health Service Hospital.

consisted of a nurse and two aides; the evening shift, a nurse and an aide; the night shift, a psychiatric aide.

After the presence of physical dependency had been established, methadone hydrochloride syrup was given in sufficient quantities to control the signs of withdrawal. The amount of methadone required was determined by a standardized empirical method.* Once the stabilization dosage was established, the patient was maintained on this amount of methadone for three consecutive days. The amount of methadone hydrochloride was then decreased daily by 10 mg. until the patient received 5 mg. twice daily. The following day he was given his last dose of 5 mg. of methadone hydrochloride, and the drug was then discontinued.

The pharmacist was supplied with tablets containing 400 mg. of meprobamate per tablet and with identical tablets of a completely inert placebo. These tablets could not be differentiated by taste, smell, consistency, or appearance and were supplied to the ward in containers labeled A and B. The pharmacist was the only one who knew their identity until after analysis of the data was completed. One group of patients received meprobamate—one tablet at 10:00 a. m., one tablet at 2:00 p. m., and two tablets at bedtime. An identical dosage schedule was carried out with placebo. If a patient asked about the nature of his medication, he was told: "This is a part of your withdrawal routine." All tablets were discontinued upon completion of the methadone-withdrawal regimen. The third group of patients on the methadone-withdrawal regimen received no additional medication. Excluded from all groups were drugs affecting sleep (hypnotics and sedatives), tranquilizers, and drugs affecting muscular pain, such as salicylates.

Measurements consisted of a series of scales devised to objectify judgments about certain aspects of the withdrawal syndrome. All these scales, with the exception of the Himmelsbach scale for measurement of withdrawal signs, were developed by us. Observations were made by the staff for two weeks prior to initiation of the study. This familiarized the staff with the scales, established interjudge consistency, and a stable ward routine.

The ward physician recorded his observations each day at the same time on every patient. His observations were made as follows:

1. "Withdrawal signs." We utilized the Himmelsbach scale, a clinically developed method for evaluating opiate withdrawal, in which the severity of signs is graded on a five-point scale.[8]

2. "Sleep, subjective." The patient was asked: "How did you sleep last night?" If he complained of restless, fitful, or uncomfortable sleep, a positive answer was recorded. If he stated that he slept well and had not awakened during the night, a negative response was recorded.

3. "Muscle tension, objective." This measurement was rated according to a three-point scale: 0: No evidence of any discomfort. Examination of muscles revealed no twitching, fibrillation, or muscle spasm. 1: Evidence of moderate discomfort. The patient might sleep on the floor or a hard surface and curl himself into odd positions. Palpation of muscles revealed the presence of definite muscle spasm. 2: Evidence of marked discomfort. There might be twitching and kicking motions of the extremities. Palpation revealed the presence of severe muscle spasm and tenderness.

4. "Muscle tension, subjective." The patient was asked: "How do you feel?" His responses were recorded on a four-point scale. If he replied to the question by complaining of severe muscle pains, he was rated as 3. A rating of 2 was recorded

* A patient, for example, enters the hospital one morning, stating that he is addicted to morphine, that he had his last medication the morning of the previous day. At the time of admission he manifests no definite withdrawal signs. Several hours later, however, he is noted to display withdrawal signs, such as goose flesh, lacrimation, rhinorrhea, and dilated pupils. At this time he is given 15 mg. methadone hydrochloride syrup. After observation one hour later it is found that withdrawal signs still persist. The patient is then given an additional 15 mg. of methadone hydrochloride syrup. On subsequent hourly observations throughout the day and night the patient manifests no definite withdrawal signs. The following morning he is observed by the physician to have moderate withdrawal signs. He is then placed on a stabilization dosage of 20 mg. of methadone hydrochloride twice daily. Stabilization doses of methadone hydrochloride ranged from 20 to 70 mg. daily. The average dose was 45 mg. daily, equivalent to approximately 140 mg. of morphine.

when the patient complained of mild muscle pain. If the patient did not respond with a complaint about his muscle symptoms, he was then asked: "Do you have any muscular pains?" If he responded to this by complaining of severe muscle pains, he was rated as 2. A rating of 1 was recorded when he complained of mild or moderate muscle pains. A completely negative response was rated as zero.

Two sets of observations were made each day by the nursing staff. A nurse and psychiatric aide on both day and evening shifts submitted observations, each pair submitting a single set. The scales on which ratings were made were as follows:

1. "Sleep." At hourly intervals throughout the night, a light would shine on each patient to ascertain whether he was sleeping. The total number of hours of sleep was recorded each morning.

2. "Appetite." A three-point scale was used, each patient's appetite being evaluated as "average," "markedly increased," or "markedly decreased." The standard used was the rater's concept of an average person's appetite during withdrawal.

3. "Talkativeness." Each patient was rated on a three-point scale as "very quiet," "average," or "very talkative." The standard in this case was "people in general."

4. "Well-being." A three-point scale was used, each patient being rated as "unhappy," "average," or "euphoric." The standard in this case was "people in general."

5. "Motor activity." Each patient was rated on a five-point scale as "lethargic," "hypoactive," "average," "hyperactive," or "very restless." The standard used was "people in general."

6. "Involvement with others." A five-point scale, describing each patient as "seclusive," "indifferent," "average," "outgoing," or "overly involved," was used by the observers. "People in general" was used as the standard.

7. "Attitudes toward others." Each patient was rated on a five-point scale as "overly hostile," "uncooperative," "average," "cooperative," or "overly friendly," the standard being "people in general."

8. "Acting-out behavior." A three-point scale was used describing the patient's acting-out behavior as "none," "moderate," or "marked." The standard in this case was "people in general."

Ratings by the day- and evening-shift observers were treated separately in the statistical analysis of the observations.

Results

The results were subjected to statistical analysis. Certain weaknesses appeared in the measurement which necessitated the use of nominal data statistics on ordinal data. This was due to insufficient variability in many of the observations. A limited range of observations was considered to be justified where the observations were of clinical significance. Throughout the analysis, differences among groups which attained the 0.05 level of significance were interpreted as not having occurred by chance.

The Population Measures.—The three groups of patients were tested for homogeneity on several vital data and on one withdrawal measure. Table 1 shows the results of these analyses.

TABLE 1.—*Population Measures* *

Measure	Range	Average	Test†	α ‡	Null Hypothesis: Accept	Null Hypothesis: Reject	Direction of Difference
Age	19-67 yr.	30 yr.	Extension of the median test for k independent samples	$\alpha > 0.10$	x		
Duration of addiction	1-48 mo.	8.4 mo.	χ^2-test for k independent samples	$\alpha = 0.90$	x		
Total years of addiction	A:3-40 yr. B:1-10 yr. C:1-20 yr.	10.85 yr. 5.00 yr. 6.43 yr.	Extension of the median test for k independent samples	$\alpha < 0.01$		x	
			Extension of the median test for 2 independent samples				
			A *vs.* B	$\alpha < 0.01$		x	A > B
			A *vs.* C	$\alpha = 0.02$		x	A > C
			B *vs.* C	$\alpha > 0.01$	x		
Methadone	20-70 mg.	43.9 mg.	Kruskal-Wallis one-way analysis of variance	$\alpha > 0.05$	x		

* A = meprobamate; B, placebo; C, control.

† α = level of significance of differences.

Column 1 lists the four measures of population homogeneity which were employed. The statistical test applied in analysis of the differences among the groups is shown in Column 4. Column 5 lists the level of significance of the differences among groups. Acceptance or rejection of the null hypothesis according to the criterion of the 0.05 level of significance is recorded in the sixth column. In those cases where significant differences appear, the direction of the difference is indicated in the last column. It is noted that the three groups are homogeneous in all measures except years of addiction. The measure of age in the groups was treated dichotomously. Duration of current addiction was measured in months, and the data were treated dichotomously. The two ranges extended from 1 to 6 months and from 7 to 48 months. The methadone dosage was subjected to a nonparametric one-way analysis of variance.

Significant differences did appear among the groups on the basis of total years of addiction. In this measure subjects were treated dichotomously. The difference among the groups was tested in terms of the number of subjects in each group falling above and below the median number of years for all of the subjects in the study. It is noted that the meprobamate group is significantly longer addicted than the placebo and control groups, while the placebo group is not significantly different from the control.

The Experimental Measures.—The range of observations on the scales was generally small, both because of the construction of the scales and because judges tended to avoid extreme ratings. In several instances there was insufficient variability in the ratings to justify application of statistical tests to analysis of differences among groups. With one exception, the statistical tests employed treated the data as frequencies in discrete categories.

Table 2 shows four instances in which the null hypothesis was rejected in favor of the experimental hypothesis. On the "withdrawal-signs" measure, it is observed that the placebo group showed significantly severer withdrawal signs than the control group. While a five-point scale ranging from 0 to 4 was used in the observation of withdrawal signs, the data were treated dichotomously for analysis of the differences among groups; i. e., the data were recast to show whether a subject did or did not show withdrawal signs.

The second significant difference which appears is on the "objective muscle tension" scale. Here it is observed that the meprobamate group showed significantly more objective muscle tension than did the control group, a difference which is significant at the 0.01 level. Data in this case were treated dichotomously, having been recast to indicate whether a subject did or did not show objective muscle tension.

The third and fourth significant differences which appear are on the "subjective muscle tension" scale. Here it is observed that both the meprobamate and the placebo group experienced more muscle tension than did the controls. These differences were significant at less than the 0.001 level and less than the 0.01 level, respectively. No other significant differences appear among the analyses.

While the same scales were applied to patient's behavior by the day- and evening-shift nurses, it is noted that some scales included in the statistical analysis for one shift are not included for the other, and that some scales have been eliminated from the analysis. This occurs in instances where there was insufficient variability in the observations to meet the requirements of any statistical tests. In those instances in which the statistics were applied, however, it can be assumed that the level of significance is accurate, since the measures did not meet the theoretical requirements of the statistics applied.

General Observations.—No serious side-effects of meprobamate were noted except for four patients who had mild skin eruptions accompanied by pruritus. Patients

TABLE 2.—*Experimental Measures* *

Measure	Test †	α ‡	Null Hypothesis: Accept	Null Hypothesis: Reject	Direction of Difference
Withdrawal signs	χ^2-Test for 2 independent samples				
	A *vs.* B	0.10> α>0.05	x		
	A *vs.* C	0.10> α>0.05	x		
	B *vs.* C	α<0.001		x	B>C
Sleep (subjective)	χ^2-Test for 2 independent samples				
A: 105 positive instances	A *vs.* B	α>0.05	x		
95 negative instances	A *vs.* C	α>0.05	x		
	B *vs.* C	α>0.05	x		
B: 116 positive instances					
86 negative instances					
C: 100 positive instances					
93 negative instances					
Muscle tension (objective)	χ^2-Test for 2 independent samples				
A: 33 positive instances	A *vs.* B	α>0.10	x		
160 negative instances	A *vs.* C	α<0.01		x	A>C
	B *vs.* C	α>0.10	x		
B: 24 positive instances					
179 negative instances					
C: 15 positive instances					
178 negative instances					
Muscle tension (subjective)	χ^2-Test for 2 independent samples				
	A *vs.* B	α>0.10	x		
	A *vs.* C	α<0.001		x	A>C
	B *vs.* C	α>0.01		x	B>C
Sleep (objective)	Kolmogorov-Smirnov 2-sample test for large samples				
	A *vs.* B	α>0.05	x		
	A *vs.* C	α>0.05	x		
	B *vs.* C	α>0.05	x		
Range, hr. Average, hr.					
A: 0-8 5.55					
B: 0-8 5.58					
C: 0-7 5.35					
Well-being	χ^2-Test for *k* independent samples	α>0.30	x		
Motor activity (day)	χ^2-Test for *k* independent samples	α>0.10	x		
Involvement with others (day)	χ^2-Test for *k* independent samples	α>0.90	x		
Talkativeness (day)	χ^2-Test for 2 independent samples				
	A *vs.* B	α<0.001		x	A>B
	A *vs.* C	α>0.05	x		
	B *vs.* C	α<0.01		x	B<C
Talkativeness (night)	χ^2-Test for *k* independent samples	α>0.30	x		
Well-being (night)	χ^2-Test for *k* independent samples	α>0.50	x		
Motor activity (night)	χ^2-Test for *k* independent samples	α>0.30	x		
Involvement with others (night)	χ^2-Test for *k* independent samples	α>0.50	x		

* A = meprobamate; B, placebo; C, control.
† α = level of significance of difference.

undergoing withdrawal have been commonly described as manipulative, demanding, histrionic, unreliable, complaining, and emotionally unstable.[8] It was therefore anticipated that the subjects would question the staff about the nature of the medication received, why some patients received medication and others did not, and would make attempts to obtain more medication during the withdrawal procedure or continue its use beyond the period of withdrawal. In no case did this eventuate. The subjects accepted the explanation that the pills were "part of withdrawal," manifesting no desire to continue their use at the termination of the methadone regimen.

Conclusion

Meprobamate is not of value as an adjunct in the management of the opiate-withdrawal syndrome, as determined by this study.

Comment

A negative placebo effect was observed in this study. Patients who received the placebo manifested significantly more withdrawal signs, more subjective muscle tension, and were less talkative than the control patients. In no instance were they more comfortable than patients on the methadone regimen alone. Those receiving meprobamate also appeared negatively affected as compared with the controls. They manifested more objective and subjective muscle tension than did the controls. Like patients receiving placebo, those on the meprobamate regimen were not improved as compared with controls. The only area of significant difference between the drug and the placebo group was in talkativeness, the meprobamate group appearing more talkative.

This study indicates again the effectiveness of the methadone substitution method in alleviating the objective and subjective responses of an opiate addict undergoing withdrawal. The reputation of the hospital, ward setting, standardization of the regimen, and presence of a stable, sympathetic, and experienced ward staff have all undoubtedly played roles, along with the inherent effect of the methadone. The addition of a placebo or an apparently ineffective drug exerted an adverse subjective effect in both cases and affected objective muscle spasm inimically in the case of meprobamate. We feel that the explanation of this lies in the nature of our subjects, their knowledge and expectations of drugs. As a sophisticated group in terms of drugs and their effects, they estimated the pills to be of little benefit to them. We can thus understand their lack of interest in the nature, dosage, and duration of this medication. Expecting additional effects from the "new" medicine, they may have expressed their feelings of disappointment by an increase in subjective complaints. Another explanation may lie in the fact that patients receiving meprobamate or placebo believed that the staff considered them "sicker" than patients on the methadone regimen alone. They may therefore have expressed more complaints to comply with what they considered to be the staff's expectations. We are unable to account for the increase in objective muscle tension in the meprobamate group. This may also be associated with the negative placebo effect or may be due to a parodoxical physiological response to meprobamate in the opiate-withdrawal syndrome. A possible relationship is the reported excitant effect of meprobamate on mice.[9] The entire problem requires further investigation, such as comparison of meprobamate with a drug of known effect, e. g., barbiturate. In our hospital milieu, patients undergoing treatment for withdrawal were comfortable, cooperative, and amenable to treatment. They did not manifest the manipulative, demanding, and acting-out behavior patterns commonly described.

The opiate addicts in the three groups were samples of a homogeneous population as measured by age, drug used, duration of current addiction, and severity of addiction. Patients in the meprobamate group had used drugs for a longer period of time than those in the other groups, and this fact might have adversely influenced their responses to the medication. However, a review of the literature and expert opinion[10] indicate that this is not a significant factor affecting response to opiates. It is further observed that the differences among groups were not of great clinical magnitude. Our over-all subjective impression is that there were no gross differences in withdrawal symptomatology among the groups, although a tendency to negative placebo effect was found. Greater differences may have been found if not the methadone substitution method, but meprobamate, placebo, and unmodified control, had been used. Because of the discomfort and potential danger of an unmodified withdrawal syndrome, the investigators felt that this procedure was not justified in our hospital setting. In this study methadone was substituted for all other opiates and then withdrawn at a standardized rate.

Summary

A controlled clinical study was devised to test the hypothesis that meprobamate will favorably influence the opiate-withdrawal syndrome. Sixty-two patients were divided into three experimental groups. Using the methadone substitution method of withdrawal, the effects of meprobamate and placebo were compared with the control on aspects of the withdrawal syndrome. Results indicate that meprobamate is not of value as an adjunct in the management of the opiate-withdrawal syndrome, as determined by the study. Placebo or ineffective drugs may adversely affect treatment of opiate withdrawal.

U. S. Public Health Service Hospital, P. O. Box 100.

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Books

BOOK REVIEWS

Social Class and Mental Illness: A Community Study. By August B. Hollingshead and Fredrick C. Redlich. Price, $7.50. Pp. 442. John Wiley & Sons, Inc., 440 Fourth Ave., 1958.

The ten-year collaborative research directed by Hollingshead, a sociologist, and Redlich, a psychiatrist, has already produced some twenty-five papers; and the general drift of their work is very well known. But in "Social Class and Mental Illness" most of the major data of their project are given for the first time in detail. (A second volume, entitled "Social Class, Family Dynamics, and Mental Illness," by Jerome Myers and Bertram Roberts, will soon be published.) The entire project represents trends of capital importance that are affecting the nature and destiny of psychiatry.

One trend is the sociologizing of psychiatric research—meaning the incorporation of sociological perspectives into the study of mental disease and its treatment. The parallel and conjoint researches of sociologists and psychiatrists have supported the movement toward a social psychiatry, itself a close relative of what has come to be called, rather broadly, of course, "milieu therapy." All of this increasing emphasis upon the possible (its supporters claim, the actual) importance of social factors in mental illness is itself linked with the continuous change in the position of psychiatry itself as a profession. If psychiatry were a stationary profession, a stable occupation, the mandate of the psychiatrist as society's chief agent for dealing with the mentally ill would be fixed for once and for all. But an increasingly concerned civil conscience, abetted by a rising standard of living—rising in what some observers have called a new kind of economy of nonscarcity—has begun to call for concerted attack upon our massive problem of mental illness; and this has meant that a number of other specialist occupations have gotten into the psychiatric act, either as supplementary agents or as challenging agents to psychiatrists in the diagnosis and treatment of mental patients. This kind of picture is probably no less true of any medical specialty, except that in the case of psychiatry the challenging and supplementary approaches have also come from the behavioral sciences. Moreover, with psychiatry itself split among practitioners who lean toward somatic treatments, toward various psychotherapeutic treatments, and toward milieu treatments, it was inevitable that sociologists and anthropologists would join the procession of nonphysicians who were legitimately concerned with mental illness. Their participation is made all the easier by the calls from within psychiatry itself either to abandon or to improve the large state hospitals as centers for treating our great population of the mentally ill.

The Hollingshead-Redlich book is, from one point of view, a report of a well-designed, carefully carried-out research into the influence of social class upon the prevalence and treatment of mental illness. ("The research reported here focused upon two questions: Is mental illness related to social class? Does a mentally ill patient's position in the status system affect how he is treated for his illness?" The answer is an unequivocal affirmative for both questions.) From another point of view, the report can be seen, and should be judged, as an effective rhetoric designed to turn psychiatrists toward a much more socially oriented perspective. The authors know their own intent, and have consequently offered their readers both a clear presentation of their data and research conclusions and some frankly exhortatory programmatic prose. The latter is fully as important, I believe, as the research presentation itself.

If the reader is especially interested in the research side of the volume, he will very likely find certain chapters of particular value. The early chapters, gathered together in Part Two ("The Social Setting"), describe something of the history of New Haven, its social classes, and the city's psychiatric facilities. The latter part of the chapter on psychiatric facilities is especially noteworthy for its description of private practitioners, who are typed as those leaning toward a predominantly analytic and psychological orientation, and those with a directive and organic orientation. The training, orientation, practice, and style of life of both types of practitioner are very effectively laid out for us.

Chapters Six, Seven, and Eight, which together comprise Part Three, are perhaps the heart of the research presentation. For it is here that the authors present material bearing upon their

two major hypotheses: namely, that (1) the prevalence of treated mental illness is related significantly to an individual's position in the community's class structure, and (2) that the types of diagnosed psychiatric disorders are connected significantly to the class structure of the community. The first hypothesis is attacked in terms of the paths taken by patients to the psychiatrist: How do they get to the psychiatrist? Who refers them? The crucial tables are given on pages 186 and 187. In general, it is apparent that there exist sharp class differences in the source of patient referral. For instance, Classes I and II, at the top of the social scale, scarcely ever get referred via social agencies or the police and the courts, whereas Class V, at the bottom of the social heap, gets frequently "referred" by these institutional agents of society. And there are some differences between how neurotics and psychotics get referred, although social-class differences obtain for both kinds of patients. There are some nice questions raised by these tables. One is: Who does not get to the psychiatrist at all because he is not (for instance, in the fifth class) defined as ill either by the police or by the social worker? Another is: Just who is likely to come to the attention of these agents, and who it not, and who can plead off despite such attention? Another is: How does Class IV manage to escape so well some of the mandated surveillance of those agents? Another is: Where do some mentally ill, as defined by themselves or others, take their troubles besides to the psychiatrist? (Hollingshead and Redlich make clear, also, that they are talking only about the paths between the point at which a decision for psychiatric treatment is indicated and a later point, when the decision is implemented by the contacting of a psychiatrist by the disturbed person. They give us no data on what they call the first two milestones that precede these points, namely, the occurrence of abnormal behavior and the appraisal of the person's behavior as disturbed in the psychiatric sense.) In Chapter Seven, the authors handle the question of social class as it relates to the prevalence of disorders. Prevalence is defined as "the number of cases of a specified disease present in a population aggregate during a stated interval of time." They are aware of the difficulties of using prevalence to check upon the amount of disease in relation to social class: They are willing to settle for "treated disease," rather than actual disease. They conclude: (1) A definite association exists between class position and being a psychiatric patient; (2) the lower the class, the greater the proportion of patients in the population, and (3) the greatest difference is between Classes IV and V in that Class V has a much higher ratio of patients to population than does Class IV. In short, the lower down in the social scale, the more contribution is made to our mentally ill treated population. (The question, of course, is now translatable into this: Is there actually more mental illness the lower down in the social scale one goes, or are the reported figures in large part a reflection of the nature of the referral system in America? To raise this question is not to cavil but to ask, rather, for some further attack upon an exceedingly important problem.)

After a chapter devoted to examination of types of psychiatric disorder by social class, the authors give us another excellent chapter on who gets what type of treatment, where, and for how long, broken down for social class and types of patient (neurotic, psychotic) especially. Again, their sociological viewpoint leads Hollingshead and Redlich to postulate that the type of treatment a patient receives will be connected with his class position; and this is what they prove. The proof here is especially convincing, too. Psychotherapeutic therapy is used "in disproportionately high degrees" with the higher-status neurotic patients treated by private practitioners, whereas the organic therapies "tend to be applied most often to neurotics in Classes III and IV." For psychotics, differences of therapy are "most marked for the schizophrenics, contributing, in no small part, to the large number of chronic patients in Class V who remain in state hospitals year after year." The bulk of patients with affective disorders receive electroconvulsive treatment, leading the authors to conclude: "This suggests that if, for a given disorder, there is a treatment available which is relatively effective, inexpensive, and technically simple, class differences may be reduced, but not eliminated." (In other words, when a treatment really seems to work, by general agreement, then class differences obtain much less—incidentally, a nice argument for a somatically oriented psychiatrist to seize upon.) The following chapter makes plain why there exist some of these great differences in treatment per class: It deals with expenditures on treatment. This is a particularly nice chapter, for it establishes beyond question the differential chances that the various social classes have for purchasing various well-thought-of and prestigeful types of therapy. The chapter also brings out the relevance of social class for public expenditures on state hospitals. In Classes II and III, patients are sent there as a last resort, "and usually only after their families have exhausted their resources in private facilities." Class IV uses these institutions as treatment centers, as

well as for custodial care. But the state hospital—and this is an important point for the authors' later argument—"is the one psychiatric facility available to Class V persons who become so disturbed that they have to be separated from the community." The state hospital is a minimum-cost institution on a per diem basis, but a maximum-cost institution in the long run, they contend, because it is a dumping ground for psychotic patients of Classes IV and V, and especially for the latter.

Although some of the burden of the authors' argument is carried along in the research chapters, it comes out more explicitly in Part Five, which section is devoted to discussion and application. As they say, here they will review the state of research in social psychiatry critically and put forth controversial proposals. Actually, they are putting forth proposals which are controversial to psychiatry proper rather than just to social psychiatry. For one thing, they argue that, since the lowest class, Class V, contributes such a disproportionate number of treated patients and gets so little chance at the more advanced psychotherapies and at the more progressive psychiatric institutions, then something is radically wrong with psychiatry. And something should be done about it. This position assumes that what should be done about it—at least in considerable part—is to develop ways of reaching the lowest class more effectively with psychotherapeutic and milieu-therapeutic methods. But within this frame of reference Hollingshead and Redlich make very effective criticisms of the present state of psychiatric practice. Psychiatrists do not reach the lower two classes—partly because of the organization of the profession, partly because of the financial plight of these classes, partly because of the barriers of communication that exist because psychiatrists do not derive from those classes, and partly because these classes do not understand what mental disease is all about.

Some of the finest pages in the book deal with these lacks and with an appeal to the social conscience of the profession. They call for new methods of treatment which will give lower-class patients an essentially fairer chance to recover than they now have. They ask for much more research into the specific problems of the lower classes—by social scientists, as well as by psychiatrists. (The key sentence here is: "Class V needs help most—social and psychiatric—and gets it least.") This means that, among other things, sociologists should be appointed to major staff positions in departments of psychiatry wherever residents are in training; and so we shall develop a new kind of psychiatrist. What this all means is that social science should not enter late into the process of the adult psychiatrist's life, but early; not just that social scientists should work collaboratively with psychiatrists, but that psychiatry should co-opt social science into its training in order that its practitioners and researchers have new multiple skills and perceptions. This is still quite a radical argument, and, of course, there is some question whether the movement will fade away or get institutionalized. It seems likely that institutionalization will occur, for in a way this rediscovery of the lower class is a recapitulization, some seven or eight decades later, of the discovery of the physical, medical, and educational needs of the submerged urban classes by middle-class reformers—except that this time mental illness is at the focus of concern.

But, as I have by now made clear enough, this research gives rather powerful support to that movement, and especially to those members of it who are most concerned with treatment upon a more massive national basis than now exists. It seems to me that the actual research conclusions—and the data on which they are based—ought to be scrutinized carefully against this context of social movement. (For instance, the differences between Classes IV and V are sometimes maximized in the book, just because V is our most underprivileged class generally, and the authors are particularly concerned that their readers see this.) But the book is altogether a notable achievement.

ANSELM STRAUSS, Ph.D.

Juvenile Delinquency. Edited by Joseph S. Roucek. Price, $10.00. Pp. 370. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1958.

In the preface, the editor says: "The following chapters suggest that the adequate understanding of criminal behavior is based on the theory of multiple causation, that it is always a combination of causes which produces juvenile delinquency, and that this combination varies from one case to another. This approach of this book conduces to a realistic appraisal of the many factors at work in the generation of juvenile delinquency, and cautions against the easy type of overgeneralization frequently found among those who attribute crime to a single cause, such as 'the parents are to blame,' 'slum conditions are the cause of crime,' or 'the lack of educational facilities is the cause of all troubles'." From a first reading, one might expect that the problem will be looked at and presented from a multidisciplinary, multicausal frame of

reference, or perhaps even from a transactions-processes reference; but if this is the expectation after perusing the quoted sentences, the reader is, as was the reviewer, doomed to disappointment.

The format of presentation divides the book into four sections: The first deals with a definition of the problem; the second, with a search for causes; the third, with evaluations of attempted solutions, and the fourth, with international trends. Some of the papers emphasize the difficulty in the evaluation of incidence statistics because of the wide discrepancies in the methods of reporting. Other excellent papers present the legal definitions of delinquency, pointing up their contradictoriness and paradoxicalness, and would be amusing were the problem not so serious and potentially devastating. The confusions, limitations, and rights-depriving aspects of juvenile courts and the ways in which they are administered are very clearly set forth. Several papers show very explicitly that the problem is not "juvenile delinquency," but, rather, is one of delinquent juveniles; that each case has factors which differ from those in every other case, and that each one must be handled on an individual basis.

In the second section, the chapter headings are "The Biological Basis of Juvenile Delinquency," "A Critique of the Psychiatric Approach," "Sociological Processes," etc. In a group of papers dealing with a search for causes what valid position is occupied by a critique? If critiques are being offered, why are causes being searched? The paper on a psychiatric critique is a naive and confused one. It appears that the author has used his paper as an excuse for an exercise in antipsychiatric polemics without bothering to explore the possibility that psychiatry has made positive contributions to the attempt to understand juvenile delinquents. This paper seems very much out of place with the others.

There are fourteen papers presented; ten of them are authored by people in the field of sociology, two by people in academic case work, one by a worker in social psychology, and one by a newspaper reporter. Missing are authors in the fields of clinical case work, clinical psychology, psychiatry and/or psychoanalysis, probation, teaching, e. g., a high school principal, and law. It would seem that a multiple-causation approach should include some of the above-mentioned fields, and not just different ideas presented primarily from the field of sociology. A unidisciplinary presentation, and the reviewer feels that, with the exception of the newsman, all the authors can be subsumed under the general field of sociology, can be repetitious, and this is actually the case, with the same ideas presented again and again in slightly different wordings.

It appeared to this reviewer that the audience for whom this book was intended was one primarily in the field of sociology and might therefore prove quite disappointing to students in the other disciplines, whose representing authors are made very conspicuous by their absence.

In this day, with the problems of juvenile delinquents made increasingly more evident by newspaper accounts and police and court statistics, and with the need for ways of dealing with the problems becoming daily more urgent, new, fresh-sighted approaches are needed; contributions from serious thinkers and clinicians in many fields are desired, but, unfortunately, "Juvenile Delinquency" provides none of this.

CHARLES H. SHAIOVA, M.D.

Remotivating the Mental Patient. By Otto von Mering and Stanley H. King. Price, $3.00. Pp. 216. Russell Sage Foundation, 505 Park Ave., New York 22, 1957.

For good reasons, the literature concerned with large mental hospitals has emphasized problems, frustrations, and failures. It has become almost cliché to point out poor housing, overcrowding of patients, lack of sufficient personnel, intrastaff tensions, and various consequences of the above, including profound pessimism regarding patient recovery, and dehumanization of staff-patient transactions.

Recognizing this trend, the Russell Sage Foundation sponsored studies designed to investigate and report on positive developments. Von Mering and King have attempted to focus on encouraging signs through visits to thirty psychiatric institutions located in all sections of the United States. By extensive field-work observations and interviews with personnel, they uncovered methods which illustrate what can be done to improve patient care, especially in state hospital settings. Hopefully, these findings may be utilized as models in other institutions, and, in conjunction with other studies, this report would help in counteracting pessimism regarding patient improvement. In the authors' terms, an optimistic philosophy of patient remotivation would replace the "legend of chronicity" of mental illness which permeates so many psychiatric institutions.

The book is characterized by simplicity of style and underemphasis of technical terminology. Indeed, the authors strove to understand the ward personnel's language as part of becoming aware of the prevailing climate of opinion about patients. For example, patients were classified

in such terms as "watcher, doer, doctor-chaser, pacer, sitter, T. V. addict, ward-hero or ward-clown." Wards were given equally colorful names, such as "family-ward, museum-ward or moving-ward." That the investigators were well indoctrinated into this new vocabulary was illustrated by a tendency on their part to coin new terminology themselves. For example, they applied the name "ward-mothers" to female aides assigned to small patient groups in order to provide more contact.

Most of the book is devoted to a description of specific remotivation programs. Significantly, many of the examples were taken from wards with very disturbed patients in order to show how much can be done in such settings. Under the leadership of an exceptional aide, an effective habit-training program was carried out in one closed ward for chronic male patients. Still another aide sparked a remotivation program in a ward for elderly patients in a different hospital. The chief method utilized in this latter institution involved an attempt to foster pride by giving responsibility in as many ways as possible. However, the dedication and conviction of the charge-aide vitalized the entire program, and was probably indispensable for its success. Other examples included improvement in the treatment of postlobotomy patients by consistently utilizing any activity associated with normal living, the training of aides as section leaders ("ward-mothers"), and programs in which more effective communication was established between the hospital and patient relatives, as well as the community at large. The last was an especially vivid description of an intensive volunteer program established by a southern community, with its previously neglected state hospital.

The authors discuss the fact that most of the cited examples involve piecemeal steps, rather than an organized series of events leading to remotivation. They were unable to find an adequate example of a hospital with such an integrated program, although they cite one institution where "cafeteria-training"—their term for sequential steps leading to remotivation—was attempted. The difficulty in finding an adequate illustration reflects a major lack in psychiatric hospitals and, consequently, weakens the broader goals of the project. The isolated steps so ably described in the book must be viewed against the larger context of the state of the institution as a whole. Questions of whether or not the large hospitals can ever be improved or whether new institutional forms are required are being debated at this moment, and some resolution must be found for these questions before a truly effective remotivation program can be developed.

Many other questions were evoked by reading this book. For example, so many of the successful programs depended on unusual personal qualities of an individual. The authors describe these persons to a certain extent, but it would have been more valuable if the description of the special personal qualities had been amplified. How much does remotivation depend on implicit personality factors, as compared with explicit role definitions of various personnel? This also raises the issue of the integration of institutional remotivation programs with other treatments, such as psychotherapy and the various somatic therapies. For purposes of focusing on what can be done in very difficult settings, the authors have wisely chosen to underemphasize these areas. However, the ultimate questions of "what makes patients get better" and "why patients improve with these treatments" are basic to a full understanding of remotivation.

The authors and the Russell Sage Foundation should be congratulated on carrying out such a project. While they have not dispelled the "legend of chronicity," they have made a contribution to its eventual dissolution. Personnel responsible for the day-to-day care of disturbed patients will be especially interested in the book and find in it a large number of helpful suggestions. Others will find it to be an antidote to the extreme pessimism about state hospitals extant in much of the current psychiatric literature.

MELVIN SABSHIN, M.D.

The Psychiatric Social Worker Teaches Medical Students. By the National Association of Social Workers. Price $1.50. Pp. 64. National Association of Social Workers, 1 Park Ave., New York 16, 1957.

This pamphlet combines a group of papers by both psychiatric social workers and physicians on the use of social case workers in the education of medical students. It holds particular interest for medical educators and for those social workers who take part in the education of young doctors-to-be. The articles present brief accounts of several approaches by which a psychosocial dimension may be added to the medical student's knowledge and understanding, and, along with these, some critical discussions of the problems raised by this effort.

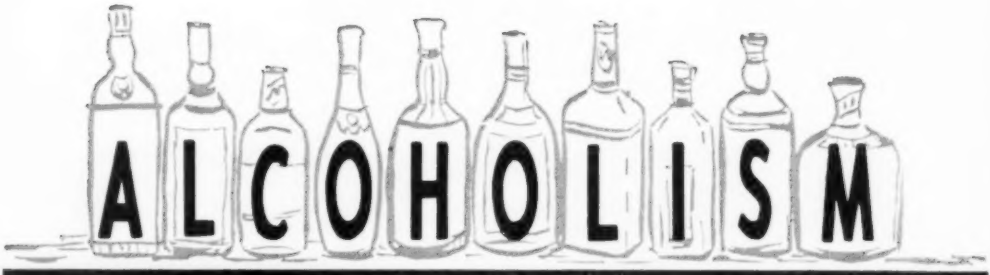
Two kinds of experience in "humanization" of medical training are reported. One is that of direct instruction by social workers; the other, that of the assignment of the medical student to "family study," which is supervised and consulted on by members of the social

service staff. In both there is evident the valiant and wholly admirable effort being made in modern medical schools to bring human significance into what might otherwise become, in the words of one of the medical discussants, "the impersonal, the anatomic, pathologic, physiologic, bacterial, pharmacological, 'scientific' view of disease entities and their treatment."

The range of teaching efforts one encounters in these brief papers reflects the responsible, and often ingenuous, thinking of both the doctors and the social workers involved in these still experimental courses. They also reflect, however, considerable need for further collaborative thinking to identify and arrive at some unanswered questions. One of these is the question of content. Summarizing the symposium on family study, one of the writers says with refreshing honesty "we glossed over the matter of content and left it to plague us in subsequent forms." And on this matter the reader, too, remains plagued. Although every writer treats of what the medical student needs to know about human beings in order to enhance his healing functions, there emerges an over-all impression of confusion—or at least lack of clarity—as to what exact content will best meet this objective. In one situation, content emphasis is upon social work as a resource which the doctor may call upon for his patients' problems in social functioning; in another it is upon certain situational and behavioral aspects of human life; in yet another, upon transmitting such case-work skills as interviewing; in most there appears a potpourri of these and of psychiatric perspectives on common human problems.

As every educator knows, the merciless limits of time in any curriculum demand a high degree of selectivity of subject matter. What is the most important kind of knowledge social work has to convey to medical students? What deserves particular focus and elaboration in this part of the medical student's education which aims to have him understand the patient as a person? What particular or unique competences does the social worker have to offer in the training of the medical student? These and other questions of specific objectives and selected content remain to be asked, and then to be answered. Perhaps the chief contribution this pamphlet makes is in the fact that by its publication it points explicitly and implicitly to the problems of focus and emphasis that are inevitable when one profession takes some part, however small, in the educational program of another.

HELEN H. PERLMAN, Ph.D.



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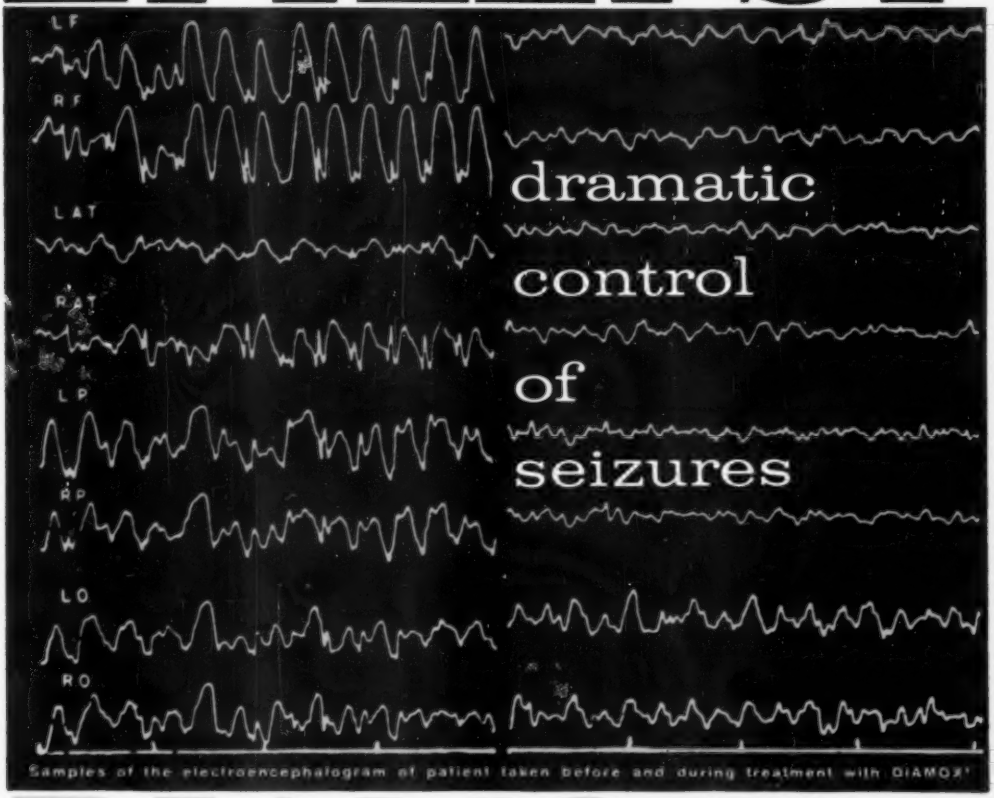

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1. Lombroso, C. T., Davidson Jr., D. T., and Grossi-Bianchi, M. L.: Further Evaluation of Acetazolamide (DIAMOX) in Treatment of Epilepsy, *J.A.M.A.* 160 268-272, 1956.

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Zier, A. and Doshay, L. J.: Procyclidine Hydrochloride (Kemadrin) Treatment of Parkinsonism in 108 Patients, Neurology (July) 1957.

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Lerner, P. F.: Kemadrin, a New Drug for Treatment of Parkinsonian Disease, J. Nerv. & Ment. Dis. 123:79 (Jan.) 1956.

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References:
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